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American Journal of Diseases of Children

VOLUME 34 DECEMBER, 1927 NUMBER 6

SICKLE CELL ANEMIA

REPORTS OF TWO CASES IN YOUNG CHILDREN IN WHICH SPLENECTOMY WAS PERFORMED *

ALBERT J. BELL, M.D., ROBERT H. KOTTE, M.D.
AND
A. GRAEME MITCHELL, M.D.
CINCINNATI
THOMAS B. COOLEY, M.D., AND PEARL LEE, M.D.
DETROIT

REPORT OF A CASE

BY ALBERT J. BELL, M.D., ROBERT H. KOTTE, M.D., AND
A. GRAEME MITCHELL, M.D.

That benefit might follow splenectomy in sickle cell anemia was called to our attention by Dr. O. H. Perry Pepper of Philadelphia. Splenectomy had also been suggested by Sydenstricker and by Huck.[1] In a previous case studied in this clinic, we had planned to carry out this procedure but after arrangements had been made, operation was refused.[2] A case that was extensively and carefully studied and in which splenectomy had been performed has recently been reported by Hahn and Gillespie.[1] For the first month following splenectomy, sickle cells could not be found in the smears, but they subsequently reappeared. Splenectomy has also been performed in a case of Dr. J. C. Gittings of Philadelphia. Great improvement followed in Hahn and Gillespie's patient, although the authors do not believe that the influence of the spleen is the cause of the sickle cell taint but that it plays a secondary rôle in the excessive hemolysis of active sickle cell anemia and is damaged in the process, passing through stages of enlargement to ultimate atrophy. To the reports of these cases we are able to add another.

History.—C. B., a colored boy, aged 18 months, was admitted to the pediatric wards of the Cincinnati General Hospital on Oct. 11, 1926, with a history of frontal headache and pain in the lumbar region of ten days' duration. His

* Received for publication, July 9, 1927.

* The report of the first case comes from the B. K. Rachford Department of Pediatrics, College of Medicine, University of Cincinnati; that of the second, from the Children's Hospital of Michigan.

1. Huck: Southern M. J. **17**:177, 1924; quoted by Hahn, E. V., and Gillespie, E. B.: Sickle Cell Anemia, Arch. Int. Med. **39**:233 (Feb.) 1927.

2. Dreyfoos, M.: Arch. Pediat. **43**:436, 1926.

neck had been stiff, and he had refused to walk. The mother attributed his illness to a fall received at the onset of these symptoms and stated that he had been well previous to this time.

The patient's birth had been normal, and the weight at that time had been 7 pounds, 4 ounces (3.3 Kg.). He had been breast-fed for nine months and had developed normally. His breathing began to be noisy shortly after birth; this condition lasted for several weeks. At times he had a dry cough and on several occasions slight convulsive seizures.

There were no other children in the family. The mother had had two miscarriages, one before and one after the birth of the patient. She had a positive blood Wassermann reaction. The father died as the result of an accident.

On initial examination, the patient was found to be well developed and nourished. The mucous membranes were pale, and the sclera had a slightly greenish tinge. A systolic murmur, interpreted as accidental in type, was heard over the pulmonic area of the heart. The abdomen was slightly distended. A large, freely movable and firm spleen extended as low as the crest of the ileum, and the edge of the liver was palpable slightly below the costal margin. All the superficial lymph nodes were slightly enlarged. The child was able to stand and walk in spite of the history to the contrary. His mentality seemed to be normal; he was alert and answered questions and obeyed commands readily. The rectal temperature of 101 F. was probably caused by an acute infection of the upper respiratory tract. The Wassermann reactions of the blood and spinal fluid were negative.

The stained smear of the blood contained a few sickle-shaped erythrocytes, and in the moist preparation there was revealed the characteristic appearance shown in figure 1. When they had stood in the moist preparation, the sickle cells always returned to normal shape, as described by Cooley.[3]

The blood of the only members of the patient's family available for examination, the mother and maternal grandfather, showed that there was no sickling of the erythrocytes in the stained or moist preparations.

On Oct. 30, 1926, about three weeks after the admission of the patient to the hospital (at 19 months of age), a splenectomy was performed by Dr. George Heuer. A preliminary transfusion of blood had been given. The reaction following the operation was satisfactory, the only disturbance being a slight rise in temperature a few days after the operation. The spleen was greatly enlarged, measuring 13 by 7 by 6.2 cm. in its greatest dimensions and weighing 186 Gm. The capsule showed old scars and was thickened. In several places, small lobulations were seen. The consistence was extremely tough, and friability was decreased. After sectioning, the cut surfaces appeared blackish-red and the coloring was so deep that it obscured trabeculations and follicular markings (fig. 3).

Microscopic Examination of the Spleen (by Dr. N. C. Foot).—"Hematoxylin-Eosin Sections: The topography of the organ is almost entirely obliterated by dense masses of erythrocytes in the pulp spaces, which are distended with blood. The capsule and trabeculae are not much altered, the splenic corpuscles are small and apparently compressed by the blood masses. The section resembles that of a blood clot in its appearance. It is a question whether this active congestion is not due to mechanical interference with the vascular supply during splenectomy—that is, whether we are not dealing with an acute passive congestion due to the ligation of the splenic vessels.

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3. Cooley, T. B., and Lee, P.: Sickle Cell Phenomenon, Am. J. Dis. Child. **32**:334 (Sept.) 1926.

Fig. 1.—Appearance of cells, showing their universal sickle shape.

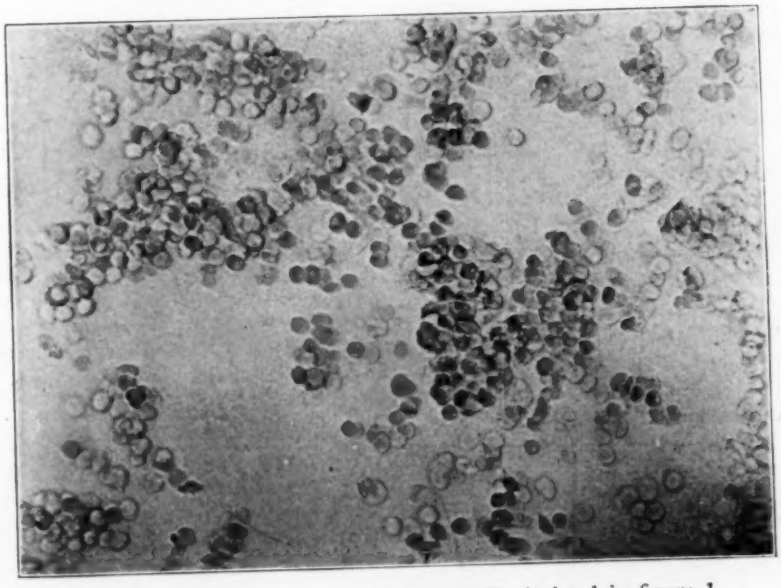

Fig. 2.—The return to normal of the cells depicted in figure 1.

"The pulp cells, aside from being crowded aside by the erythrocytes, seem quite normal. The erythrocytes show great variability in their shape, size and staining reactions; they are mostly elongated, more or less fusiform; they vary greatly in their diameter, and some stain more intensely than do others. As they were fixed in Zenker's fluid, some distortion is to be expected, but nothing comparable to what actually occurs here. Spinous filaments are suggested here and there, but not clearly demonstrable.

"Phosphotungstic Acid Hematoxylin: Here the erythrocytes are well stained and their morphology can be well made out. They show the changes already mentioned, but the distortion is now more manifest; elongation and twisting of the cells, together with definite filamentous prolongations, can be seen. The cells

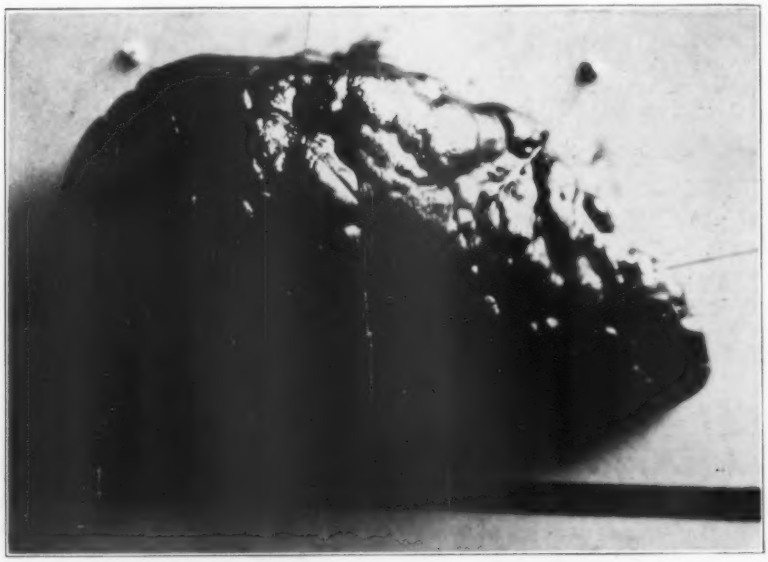

Fig. 3.—Gross appearance of the spleen.

are shaped more or less like trypanosomes, and the resemblance is heightened by the presence of the filaments.

"Bielschowsky-Maresch-Van Gieson (Foot's Modification): Here the erythrocytes are again less clearly stained, as in the hematoxylin eosin stain, but their distortion is manifest. The interesting feature in these sections is the enormous increase in the splenic reticulum, which is quite invisible in the other sections. Everywhere there is a dense interlacing felting of reticulin fibers, that seems to avoid the malpighian corpuscles, but is otherwise practically omnipresent. It merges with the collagen fibrils of the trabeculae, fading almost imperceptibly into them. The finer reticulin fibrils outline the erythrocytes in many places and enclose them intimately in a fine-meshed network. The relationship of these fibrils to the splenic reticulum is not clear" (fig. 4).

Examination of the Urine.—Albumin or sugar were never found in the urine, and microscopic examination showed nothing abnormal. Urobilin was present. Ova and parasites were not found in the stools.

Course.—The chief interest in this case centers on the examinations of the blood, some of which are shown graphically in figure 5. The anemia had shown a tendency toward improvement before splenectomy, although measures were not taken to treat it, with the exception of the usual routine hospital care and diet. Whether the improvement after operation would have occurred spontaneously is difficult to say. It seems at least possible that the temporary increase in hemoglobin and red blood cells had some relation to the removal of the spleen. Five weeks after operation, the red blood cells had increased to 4,690,000 and the hemoglobin to 85 per cent. Two months after operation, the examination showed 60 per cent hemoglobin and 3,888,000 red blood cells. Until this time, the patient seemed to be improved. He was discharged from the hospital. Six months after operation, a reexamination of the blood was made. This showed that the hemoglobin was 50 per cent and the red blood cells 1,240,000. On admission, thirty-one

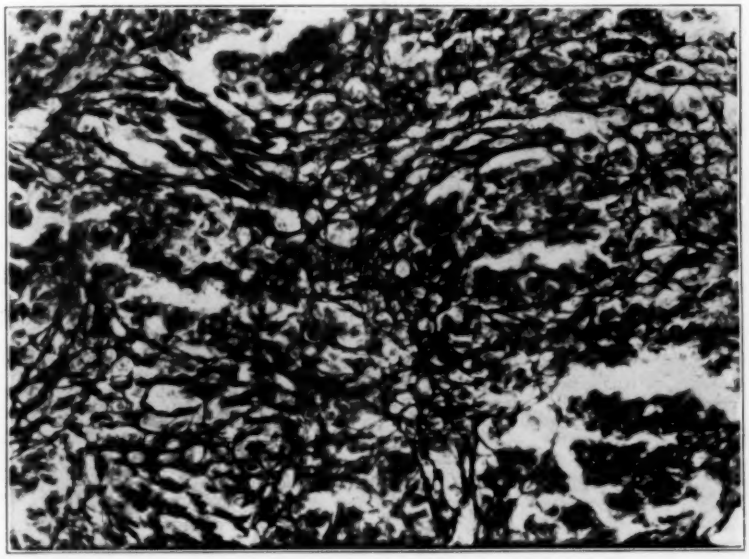

Fig. 4.—Microscopic section of the spleen; reduced from a photomicrograph with a magnification of 800 diameters. The stain used was silver ammonium carbonate, van Gieson counterstain—the technic of Foot and Menard (to be published, Arch. Path.).

nucleated red blood cells were found to each 100 white blood cells counted in the stained smear; these had decreased to twelve before splenectomy. After operation they disappeared, occasionally reappearing in small numbers later. At the examination six months after operation, the nucleated red blood cells were 69 to every 100 white blood cells counted (fig. 6). The large number of nucleated red blood cells present in the blood was of interest to us as we had observed it in a previous case of sickle cell anemia.[2] Marked anisocytosis, poikilocytosis and polychromatophilia were always present. Myelocytic cells were constantly found in all smears both before and after operation, varying from 2 to 3 up to 13 per cent. In almost all of the numerous stained blood smears made before and after splenectomy, a few sickle cells were found. In all of the moist preparations before and as long as six months after splenectomy, sickling occurred within about

three to six hours, and by from five to twenty-four hours practically all the red cells assumed the characteristic distortion. As previously stated, the sickle cells in the moist preparation always returned to normal shape after a period of from five to nine days. It was suggested that the assumption of normal form by the distorted cells might only be apparent—the appearance of the slide actually being due to a laking of the sickle cells, the previously obscured normal cells thus being revealed. We have proved on several occasions that this is not the case by serial photomicrographs taken at two day intervals, in which it was possible to demonstrate the same cells in the process of assuming normal shape (figs. 1 and 2). Once resumed, normal shape was retained. Although some slides were observed over a period of six weeks, a second sickling was never noticed. Before splenectomy the platelet count was about 300,000, and there was no change in this after operation. The bleeding and clotting times were normal before operation.

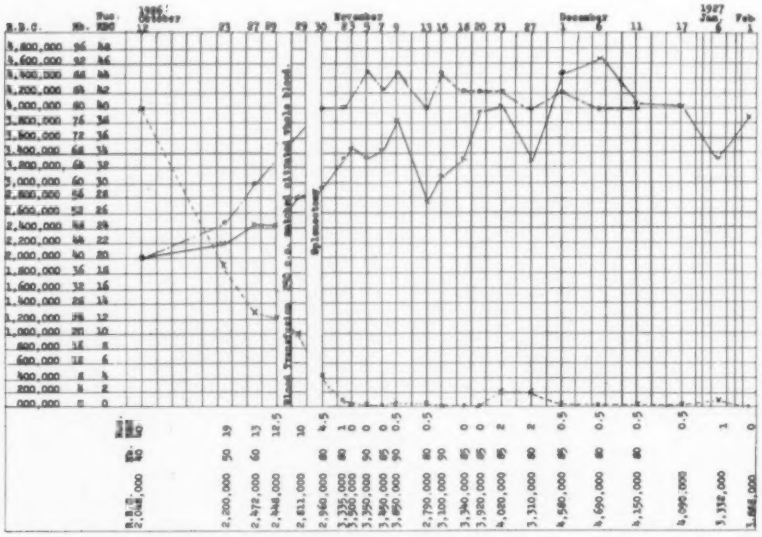

Fig. 5.—Examination of the blood in case 1. The solid line represents the red blood cells; the broken line, the number of nucleated red blood cells per hundred white blood cells in stained smear; the long and short line, hemoglobin.

The van den Bergh test, done by Dr. Schiff, always gave the indirect reaction. Before splenectomy, there were 1.37 mg. of bilirubin per 100 cc. of serum (2.75 units); immediately after, 0.55 Gm.; two weeks later, 0.63 and six weeks later, 1.0. The fragility of the erythrocytes was decreased both before and after splenectomy. One week before the operation, hemolysis began at 0.3 per cent sodium chloride and was complete at 0.2 per cent (control began at 0.38; complete at 0.3). Two weeks after operation, hemolysis began at 0.28 per cent and was not complete at 0.16 per cent, a lower dilution of sodium chloride not being used. Six weeks after operation, hemolysis began at 0.3 per cent but even at 0.02 per cent or with distilled water, hemolysis was not entirely complete. Six months after the operation, slight hemolysis began at 0.26 per cent sodium chloride and was not complete even with distilled water. The decreased fragility was apparently linked up with the number of reticulated cells present in the blood, as the nonhemolyzed cells were reticulated ones. In the blood at the time of the fragility test before

operation, there were 180,000 reticulated cells per 5 mm.; when the test was made six weeks after operation, there were 204,000 and at the test six months after operation, 268,000.

The following additional observations were made:

A. Washed red blood cells from the patient injected into a rabbit did not produce any symptoms or change in the rabbit's blood.

B. Serum from the patient likewise did not produce any symptoms when injected into a rabbit.

C. Washed red blood cells from four normal persons were mixed with the patient's serum. Sickling was not observed.

D. Oxalated red blood cells from the patient were washed eight times with normal physiologic sodium chloride solution and then were mixed with the patient's own serum. Sickling did not occur.

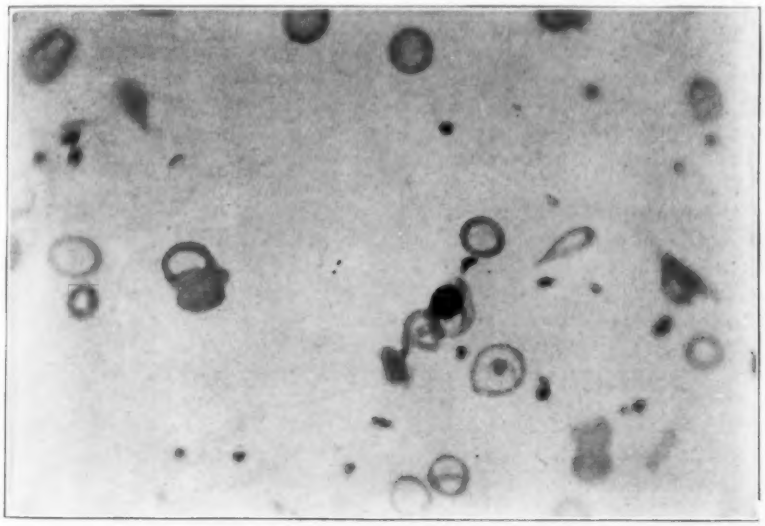

Fig. 6.—Stained smear of fresh blood with one nucleated erythrocyte and two oat-shaped erythrocytes.

SUMMARY AND CONCLUSIONS

A case of sickle cell anemia in a colored boy, aged 18 months, is reported. Splenectomy was not followed by any change in the sickling of the erythrocytes. There was temporary improvement in the anemia after operation, which may have been merely coincidental. Six months after operation, marked anemia was present.

The following observations were made in this case:

An enormous number of nucleated erythrocytes; a large number of reticulated erythrocytes; decreased fragility of the erythrocytes; the assumption of normal shape by the sickle-shaped erythrocytes on standing in moist preparations; the presence of myelocytic cells; an indirect van den Bergh reaction in the blood; failure of the erythrocytes

or serum to cause symptoms when injected into rabbit; failure of normal serum to cause sickling of the patient's cells; failure of the patient's serum to cause sickling of his own repeatedly washed cells.

REPORT OF A CASE

By Thomas B. Cooley, M.D. and Pearl Lee, M.D.

Ruth B., a colored girl, was first admitted to the hospital, Sept. 18, 1926, aged 2½ years.

The complaint at that time was of fever, abdominal pain and swelling of the feet, all of about one week's duration.

The patient was said to have had swollen and tender extremities at the age of 6 months, which condition cleared up in about two months. She had not had any other illness, and had been apparently well until the present attack.

She had been bottle fed and during the first year had received cereal, orange juice and cod liver oil. After the first year, she was given what the family ate.

The family history was negative. There had not been noticeable anemia, leg ulcers, or anything else of importance. The father, mother and an older brother were all in good health. The mother's blood showed sickling of 90 per cent of the erythrocytes after twelve hours, the father's only an occasional sickle cell.

On admission, the child was well developed and bright and was in a fair state of nutrition, weighing 12 Kg. She was apparently not ill, but had pronounced pallor of the conjunctivae and the oral mucous membrane, and greenish-yellow sclerae. The head was not unduly large, but the prominent bossae suggested antecedent rickets.

The important points in the physical examination were: moderate enlargement and chronic infection of the tonsils, with pronounced enlargement of the anterior cervical lymph nodes; slight prominence of other superficial nodes; moderate rachitic rosary; slight enlargement of the heart, with rapid pulse and soft systolic murmur; pronounced enlargement of the spleen, which extended to just above the level of the umbilicus, and seemed unusually firm; slight enlargement of the liver, which was palpable two fingerbreadths below the costal margin. The swelling of the feet complained of was not found.

There was slight fever, lasting two days after admission, and apparently due to a nasopharyngeal infection.

The urine was normal, except for slight, transient albuminuria and urobilinuria. Urobilin in minute amounts was found twice in eight examinations.

Tuberculin and Wassermann tests were negative.

Roentgenograms of the skull and long bones showed neither the changes which we have reported in von Jaksch's anemia, nor any definite sign of rickets.

Examination of the blood showed: sickling: slight after one hour; from 85 to 95 per cent after twelve hours; fragility: hemolysis began at 0.42 per cent and was complete at 0.25 per cent. Hemolysis in the control began at 0.42 per cent and was complete at 0.35 per cent. The van den Bergh reaction was direct, negative; indirect, positive. The icterus index was 12. Hemoglobin was 20 per cent (Sahli); and the red blood cells numbered 976,000; normoblasts, 58,000. No megaloblasts were found. Extreme anisocytosis, with many macrocytes and microcytes was present. Poikilocytosis was moderate. Reticulation was 40 per cent. The white blood cells numbered 44,000; polymorphonuclears, 27.5 per cent; small mononuclears, 67.5 per cent; large mononuclears, 5 per cent. No abnormal forms were found. The platelets numbered 130,000.

On September 21, the patient received a direct transfusion of 240 cc. of the father's blood. The further course of the blood picture is shown in figure 7. Variations in the white cells are omitted as unimportant.

Following transfusion, the spleen diminished rapidly in size, and finally became barely palpable. The patient received the standard anemia diet, and her general condition improved steadily, so that on October 18 she was discharged, feeling perfectly well, for further observation in the outpatient clinic. It was believed that the acute anemia had been brought on by the respiratory infection, and the mother was warned that recurrence was probable, and that splenectomy might seem advisable later.

The patient remained in good condition for about three weeks, then developed another respiratory infection, and was readmitted, November 22, with much the

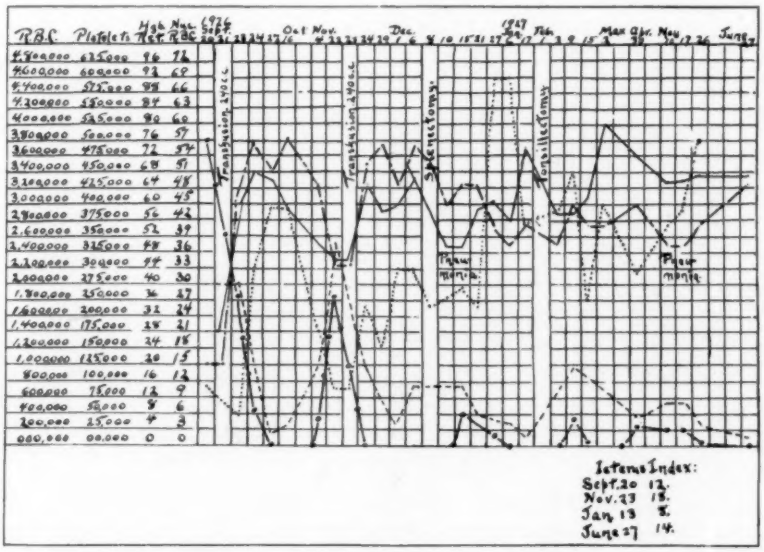

Fig. 7.—Examination of the blood in case 2. The circle dash line represents normoblasts in 100 nucleated forms; the solid line, red blood cells; the broken line, reticulation; the dotted line, platelets, and the long and short line, hemoglobin.

same complaints as before, but with a somewhat better blood picture, the hemoglobin being 45 per cent. It was decided to remove the spleen, which was again large and hard, as soon as her condition seemed favorable. Another transfusion (240 cc.) was given, and two weeks later, December 8, the infection having subsided, splenectomy was performed by Dr. Penberthy.

Immediately following the operation, the child developed a lobar pneumonia, which caused some apprehension. She went through it, however, more easily than most colored children, and made a good convalescence without further transfusion. On February 1, her tonsils were removed and on February 10, she was discharged.

On May 8 she was again admitted, with a lobar pneumonia which involved nearly the whole of the left lung, which was followed by pleural effusion. She was ill for a few days, but recovered rapidly and was discharged May 29.

As the illustration shows, the blood picture was not greatly affected by this illness, and it seemed fair to conclude that the hematopoietic system was in a less unstable condition.

At the splenectomy the spleen was found to be adherent and was difficult to remove. A small supernumerary spleen was removed at the same time. The spleen weighed 194 Gm. It was a deep purplish red and seemed firm in consistency. The capsule was thick but not wrinkled, and there were no scars. On section, no such amount of free blood could be squeezed from it as ordinarily is found in the spleen of hemolytic jaundice, and it had more the gross appearance of the spleen of von Jaksch's anemia.

In the microscopic examination, we had not the advantages of the beautiful picture given by the method of Foot and Menard, but Foot's description of the spleen in their case would answer perfectly for ours, except that in ours there was apparently more increase in fibrous tissue, due probably to the longer duration of the process. Extended description seems unnecessary.

COMMENT

Our reason for recommending splenectomy in this case was the apparent instability of the hematopoietic system, with a tendency to crises of deglobulization on the occurrence of respiratory infections. The many points of resemblance between this disease and congenital hemolytic jaundice led to the hope that splenectomy might lessen the tendency to hemolysis and might stabilize the blood picture. So far as we can judge after six months' observation, during which time the child has undergone two severe attacks of pneumonia, we think that our anticipations have been justified, though the hemoglobin and the red cells remain at a lower level than we had hoped to see. The patient feels well at this time and plays as vigorously as any child. She presents the picture of a "compensated" hemolytic anemia.

It is difficult to account for the differences in the results of splenectomy in our case as compared with those observed by Bell, Kotte and Mitchell. Possibly the fact that our patient is older, and that the disease is presumably of longer duration explains the fact that we did not obtain so great an immediate improvement in the hemoglobin and red cell count. The reappearance of the normoblasts in as great a number as before in the case reported from Cincinnati seems to indicate that the rôle of the spleen has been taken over surprisingly early by some other tissue. One wonders whether possibly a supernumerary spleen might have been overlooked.

The fact that neither in the case reported from Cincinnati nor in our own was splenectomy followed by any such erythroblastic crisis as seems to be the rule in von Jaksch's anemia is interesting, and probably indicates that the reasons for the presence of the large numbers of nucleated forms are different in the two diseases.

The lessened fragility (not changed by splenectomy), the absence of appreciable amounts of urobilin, and the high percentage of reticula-

tion in our case are all worthy of note. The platelet counts are interesting also. In the stage of acute anemia, there was no such great decrease as we have observed in our recent cases of von Jaksch's anemia; neither was there any great increase after splenectomy, though the average count has been somewhat higher. There was no diminution in the sickle cells immediately following splenectomy. In later observations sickling seems, if anything, more extreme.

CELIAC DISEASE (CHRONIC INTESTINAL INDIGESTION)

ETIOLOGY, PROGNOSIS AND STANDARDIZATION OF TREATMENT *

LOUIS W. SAUER, M.D.
EVANSTON, ILL.

Howland,[1] in 1921, established a new era in the treatment of celiac disease when he said:

> Halfway measures are quite unavailing and cause only loss of time, which is a serious matter. . . . The dietary treatment may be divided into three stages. First, that with protein milk alone. . . . That more than any other food is likely to bring satisfactory results. The diet of the second stage consists of protein milk as a basis reinforced by almost pure protein foods. The duration of this stage is many months, it may be years. . . . The third stage, that in which carbohydrates are added, is the really difficult one. The addition must be made very gradually with the most careful observation of the digestive capacity. . . . The treatment is time consuming but these patients well repay the effort expended on them. They do not remain semi-invalids. Many become vigorous and strong.

This three-phased, high protein diet is unique, because, when rigidly enforced, it is usually curative within from one to two years, sheds some light on the etiology, and has effected a favorable prognosis in this otherwise chronic disease. Gee,[2] in 1888, observed that "cow's milk is the least suited kind of food, nothing more certain"; Herter,[3] twenty years later, concluded "a strictly protein diet is most beneficial;" and Heubner,[4] in 1909, found that "the best diet is an almost exclusively protein one." In 1911, he said that in several cases he had added protein milk to the diet (which included carbohydrate foods). Ruhräh[5] then introduced soy-bean flour and evaporated milk; Lichtenstein[6] reported increase in weight in a few patients who were being fed breast milk; Still[7] said: "Fresh cow's milk is to be entirely

* Received for publication, July 15, 1927.

* From the Department of Pediatrics, Evanston Hospital.

1. Howland, J.: Tr. Am. Pediat. Soc. **33**:11, 1921.

2. Gee, S.: St. Barth. Hosp. Rep. **24**:17, 1888.

3. Herter, C.: Intestinal Infantilism, New York, The Macmillan Company, 1908.

4. Heubner, O.: Jahrb. f. Kinderh. **70**:667, 1909; Lehrb. der Kinder., Leipzig, Johann Ambrosius Barth, vol. 2, pp. 443.

5. Ruhräh, J.: Arch. Pediat. **28**:841, 1911.

6. Lichtenstein, A.: Arch. Pediat. **1**:105, 1921.

7. Still, G.: Lancet **2**:163, 193, 227, 1918; Common Diseases of Childhood, ed. 4, Oxford University Press, New York, 1924, p. 270.

forbidden, . . . many a case has done well on dried milk as the main article of diet for several years;" Haas [8] added the pulp of ripe bananas to a protein milk diet; Taylor [9] used lactic acid milk and corn syrup and Marriott [10] recommended skimmed, lactic acid milk with the curds of skimmed milk.

If spontaneous recovery (early cessation of symptoms, relatively prompt increase in weight and absence of exacerbations) is possible with each of these various diets, it is logical to assume that the celiac syndrome will disappear when carbohydrate, fresh cow's milk and fat are omitted, or are fed in amounts well below the patient's tolerance. Numerous clinicians, including Gee, Herter, Heubner, Howland, Still and Sauer,[11] have elicited prompt exacerbations by the premature or intentional addition of relatively small quantities of these three foods. This leads to the conclusion that certain noxious intestinal products are formed, probably by bacterial action on these foods. Therefore, carbohydrate, fresh cow's milk and excess of fats play an important rôle in the etiology of celiac disease.

Since signs and symptoms may develop in young children on rational diets, some clinicians have maintained that a congenital deficiency exists in gastric, intestinal or biliary secretions or ferments. The usual onset after the first year of life in children of good size and weight for their age (see charts), the catastrophic losses of weight on mixed diets rich in the three named foods and the spectacular gains in weight on the specific diet (protein milk) cannot be well explained on the basis of a congenital deficiency. Herter found a fairly typical intestinal flora with gram-positive, bifidus-like organism predominating. Brown, Courtney, Davis and MacLachlan [12] also found "a much larger proportion of gram-positive organisms, both on direct smear and on culture." They could not confirm Herter's isolation of *B. infantilis* as a separate entity, but tended rather to agree with Noguchi's observations [13] that a single, pleomorphic organism (*B. bifidus*) is characteristic. It has not

8. Haas, S.: Value of Banana in Treatment of Celiac Disease, Am. J. Dis. Child. **28**:421 (Oct.) 1924.

9. Taylor, R.: Celiac Disease, Am. J. Dis. Child. **25**:46 (Jan.) 1923.

10. Marriott, W., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 386.

11. Sauer, L.: Celiac Disease; Simple Three-Phased High Protein Diet, Am. J. Dis. Child. **29**:155 (Feb.) 1925. A sterile, creamlike protein milk can be made as follows: Thoroughly mix with each 15 level tablespoonfuls of protein milk powder, one level tablespoonful of barley flour; gradually add the water; stirr and boil in a sauce-pan for from ten to fifteen minutes; cool rapidly and keep in refrigerator.

12. Brown, A.; Courtney, A.; Davis, G., and MacLachlan, I.: Etiology of Chronic Intestinal Indigestion; Chemical and Bacteriologic Investigation, Am. J. Dis. Child. **30**:603 (Nov.) 1925.

13. Noguchi, H.: J. Exper. Med. **12**:182, 1910.

yet been proved that the presence of this or of any other organism is the specific, pathogenic invader of the intestine which causes the disease. None of Koch's postulates has been fulfilled. Celiac disease has never been produced in experimental animals. My feeding experiments (gavage and daily retention enemas) with the intestinal contents (from a fatal case) in sweetened milk and with the feces of children who had the severe type of celiac disease did not produce any symptoms in young *Macacus rhesus* monkeys which had been fed a preliminary diet of richly sweetened milk. The following data might serve as further circumstantial evidence in favor of a specific causative agent:

1. Celiac disease has never been encountered in an exclusively breast-fed infant.

2. Many of these little children are in relatively good health until the prodromal period, which usually occurs while they are on a mixed diet.

3. The usually immediate improvement (when anorexia is absent) is explained on the basis that protein milk produces an intestinal habitat unfavorable for the propagation of the causative agent.

4. Pathologic changes in the pancreas, intestinal wall and other organs, found at necropsy, are effect rather than cause, since they are analogous to changes found in various other chronic intestinal infections.

5. If the proper diet is maintained (phases II and III), exacerbations are absent, because the tolerance to carbohydrates improves when the specific causative factor has been completely eliminated from the intestinal canal.

6. Although celiac disease is relatively infrequent, various authors report cases in twins (Hablützel-Weber, Sauer), in sisters (Feer, Hess), in cousins and in nephews (Lehndorff and Mautner, Sauer). In this connection, I wish to report three instances which lead to the conjecture that, under propitious conditions, the disease was apparently transmitted from one child to another.

REPORT OF CASES

CASE 1.—William F. was convalescing from the severe type of celiac disease when his cousin, Mary B. (case 9), aged 2 years, visited him for several weeks in July, 1924. She had never had diarrhea, and weighed over 25 pounds (11.3 Kg.). After the children had played together for about ten days, the little girl developed an obstinate diarrhea with loss of weight and abdominal distention. When seen at the end of August, 1924, a typical case of celiac disease had developed, from which she completely recovered in the course of a year (figs. 1 and 2).

CASE 2.—Helen L. (table 2, case 13), who had a rather resistant case of celiac disease with recurrent pyelitis and persistent anorexia, had been in the hospital for several months. On her return home she played with her 2 year old cousin, Marilyn J. (case 14), who had moved across the street. The latter child had never been ill except for a slight anemia, occasional anorexia and constipation. The children were weighed on the same scale and played together in a sand-box. Within a month after the first contact, Marilyn developed diarrhea, extreme anorexia and abdominal distention. Within a few weeks, typical celiac disease had developed, from which she slowly recovered in the course of a year.

CASE 3.—Marjorie W. (table 2, case 18), a twin, aged 19 months, was brought to the office because she was suffering from an intermittent diarrhea, anorexia and abdominal distention. She had lost several pounds during the previous two months. Anorexia, anemia (20 per cent Dare), extreme abdominal distention, lassitude and copious stools led to an immediate diagnosis of celiac disease, and she was sent to the hospital; she remained there for more than a month, during which time she improved rapidly. About a month after her return home, the other

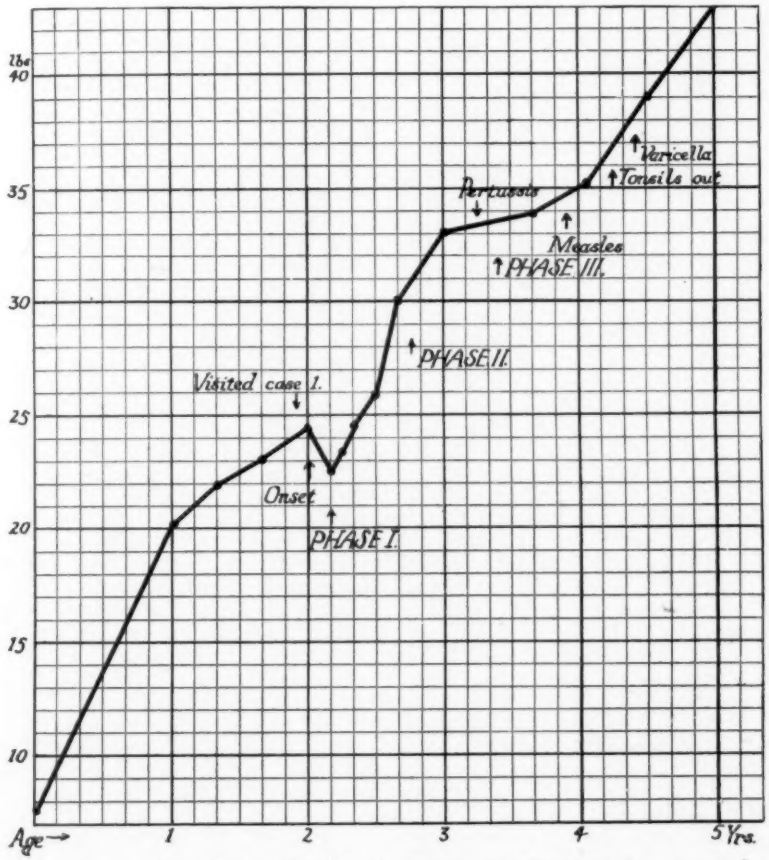

Fig. 1 (case 9).—Curve showing the course and treatment in a case of celiac disease (Mary B.). The condition began with diarrhea two weeks after a visit at the home of patient in case 1.

twin (table 2, case 19) was brought to my office, the same clinical picture was present, but in a milder degree. She was placed on a diet similar to that of her sister. Both children are doing well, but their abdomens are still prominent.

Prognosis in celiac disease depends more on the method and duration of treatment than on the severity or duration of the disease. The quality and quantity of the diet, that is, the composition of the food

is the prime factor in the course of the disease. Statistics vary greatly according to the dietary treatment (table 1) and are similar to those on the treatment of diabetes mellitus before and after the introduction of insulin. Before 1921, I used the Heubner diet in the treatment of patients who had chronic intestinal indigestion, and my results were comparable to his. The three-phased, high protein diet, which Howland used successfully in thirty cases, has been used with minor variations in twenty-five successive cases (twenty of the severe type and four of the mild type) during the past seven years. When anorexia was absent (or after

Fig. 2 (case 9).—Mary B., aged 4¾ years; weight, 41 pounds 4 ounces (18.7 Kg.); height, 40 inches (101.6 cm.); two and a half years after the onset; abdomen still prominent.

TABLE 1.—*Mortality Rate in Celiac Disease* *

Clinician	Number of Patients Treated	Per Cent Mortality
Pipping: Arch. Pediat. **3**: 342, 1924	6	50
Pirquet Clinic	5	40
Hablützel-Weber	26	23
Lichtenstein	9	22
Still	41	14
Schaap: Arch. d. mal. de l'app. digestif. **16**: 914, 1926	114 (collected)	11
Heubner	10	10
Howland	30	0
Sauer	25	0*

* A 15 month old, moribund, eczematous girl with celiac disease (weight 18 pounds [8.2 Kg.]), with a temperature of 105 F., died suddenly twelve days after treatment had been instituted. The mother had refused hospitalization. Clinical and postmortem diagnoses were celiac disease and bronchopneumonia. This child is not included in the series.

it was overcome), the improvement was rapid, complete and permanent in all but the following three instances: A moribund child (table 1, footnote) died of bronchopneumonia twelve days after the diet was begun; another child (table 2, case 11), who was anemic, had persistent

TABLE 2.—*Summary of Twenty-Five Cases in Which Three-Phased Diet Was Used*

Case	Name	Age at Onset, Mos.	Best Weight Before, Lbs.	Weight When Diet Began, Lbs.	Age When Diet Began, Mos.	Pounds Gain in Six Mos.	Complications	Subsequent Diseases	Present Age in Yrs.	Present Weight in Lbs.
1	William F....	15	23¼	16½	20	4½	Pertussis, anorexia	Chickenpox	5¾	39
2	Arthur J.....	13	20½	16¼	17	5¾	Anorexia	Measles	7½	47
3	Dorothy J...	26	26	22½	60	17¼	Spastic diplegia	Scarlet fever, measles	8½	56
4	Ann M.....	15	16¾	18⅛	20	11½	Hemoglobin 55%	Measles, tonsillitis	5¾	52
5	Catherine M.	15	22	20	19	5½	Pyelitis	Pneumonia	5¼	42
6	Marjorie S...	14	20	14½	21	14½	Hemoglobin 45%	.....	8	50
7	Jane M.....	16	23	17¾	30	15	Hemoglobin 50%, parotitis	Pyelitis, anorexia	4½	40½
8	Jean H.....	18	26	20½	33	13½	Hemoglobin 50%	None	4½	41
9	Mary B.....	24	24½	22½	26	6	Anorexia, hemoglobin 40%	Pertussis, measles, etc.	5	43
10	Stephen G....	14	25	22	19	8	Diphtheria	Measles	4	45
11	Robert S.....	14	22¼	20	16	2	Anorexia, hemoglobin 50%	Tonsillitis	2	27¼
12	Romaine S...	15	20½	19	15	5	Anorexia, vomiting	Tonsillitis	2	25
13	Helen L.....	15	22½	19½	17	8½	Pyelitis, hemoglobin 45%	Pyelitis, tonsillitis	2¾	35
14	Marilyn J....	22	23½	21	22	4	Anorexia	Anemia	3	30½
15	Robert H....	18	28	22½	22	6½	Hypothyroidism	Pertussis, measles	3½	36
16	Paul F.....	24	27	22½	28	8½	Pertussis	Measles	3¼	38
17	Robert B.....	20	23	18	26	8¼	Hemoglobin 45%	Chickenpox	4½	36
18	Marjorie W..	18	22	20	20	6¼	Hemoglobin 20%	None	2½	28
19	Martha W...	20	24	24	34	4	Anorexia	None	2½	28
20	Betty R.....	18	22	18	22	4¾	Hemoglobin 45%	Anorexia, tonsillitis	5	39½
21	Charles B....	48	35	28	48	8¼	Pirquet positive	Acidosis	8	54
22	Donald K....	17	26¼	21	17	7¾	Furunculosis	Measles, pertussis	3¾	32
23	Alfred S.....	26	28	25	26	5½	Goiter	Vomiting, colds	5	..
24	Robert M....	12	20	17¼	14	8¼	Otitis media	Diphtheria	1¾	25½
25	Carter B.....	28	35	31	31	5½	Diarrhea	Tonsillitis, chickenpox	3½	38

anorexia until he was given 75 cc. of citrated blood intramuscularly; the third child (table 2, case 12) progressed slowly owing to recurrent tonsillitis, fever, anorexia and vomiting. In all of the six original cases reported in 1924 (table 2, cases 1 to 6), the patients are at present

more or less overweight for their age; they have been free from relapses in recent years, despite numerous instances of intercurrent contagious diseases and other systemic ailments (table 2). Gibbons [14] and Lehndorff and Mautner [15] state that the prognosis in the severe type of the disease is not good. They found that bronchopneumonia, pyelitis and tetany were the most frequent causes of death. Heubner, Howland, Taylor and others remark that improvement may occur unexpectedly at times when prognosis seems most grave. Such unexpected, paradoxic reactions can be explained by the fact that the accompanying anorexia, if sufficiently extreme and prolonged, may serve per se as a spontaneous, effective cure.

The number of children "followed up" years after the cessation of the severe symptoms is small, but shows that after several years, most of those living gain in weight and in height, and at puberty are often within the limits of normalcy. Some of Heubner's patients refused or could not tolerate certain foods, especially milk. He thought that some of the cases in adults described by Schütz [16] had their origin in early childhood. It was Herter's impression that these children remained below normally physically. Hablützel-Weber found half of their living patients cured, and 40 per cent of the remainder below average physically. Most of their patients had a persistent intolerance for fat, milk and fruits. Mader [17] thinks true improvement seldom occurs before puberty. Taylor remarks that the cure of this unique disease is as mysterious as its origin.

Lehndorff and Mautner, in their recent, rather extensive monograph entitled "Coeliakie," take the fatalistic stand that no medication and no dietary regimen is likely to produce permanent results. Their experience did not include, however, a single patient treated by the Howland, three-phased diet. They state: The weight may increase and the appetite improve until suddenly, without warning, a relapse occurs. In mild cases or if the patient is not followed long enough an enthusiastic clinician might overestimate the value of treatment.

The clinical evidence collected by Howland, by Brown, Courtney and MacLachlan,[18] by Still, and by me (table 2) refutes this unfavorable prognosis.

Cognizance of the importance of accurate data on an ample number of patients under observation for a sufficient period of time led to the

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14. Gibbons, R.: Edinburgh M. J. **35**:321, 1889.

15. Lehndorff, H., and Mautner, H.: Ergebn. d. inn. Med. u. Kinderh. **31**:456, 1927.

16. Schütz, R.: Therap. Monatsch. **23**:354, 1909.

17. Mader, A.: Klin.-therap. Wchnschr. **5**:367, 1926.

18. Brown, A.; Courtney, A., and MacLachlan, I.: Brit. J. Child. Dis. **19**:113, 1922.

compilation of details on all the patients who have come under observation since 1921 (table 2). The clinical proof is now ample, as shown in the following:

1. During the protracted period of extreme anorexia, nothing is more likely to impede improvement than the inclusion or premature addition of otherwise negligible quantities of fresh cow's milk, sugar or starch; i. e., many children in the past have failed to improve promptly because the initial diet was not exclusively protein.

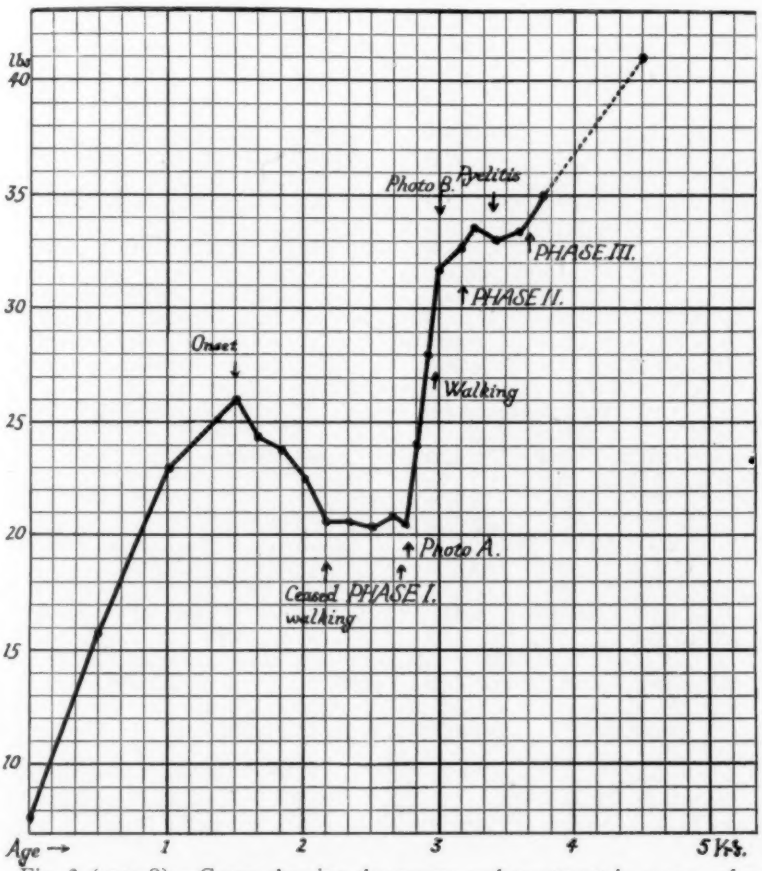

Fig. 3 (case 8).—Curve showing the course and treatment in a case of celiac disease (Jean H.); first seen at 2¾ years; weight, 20 pounds 4 ounces (9.1 Kg.); gained 8 pounds (3.6 Kg.) in fifty days.

2. Repair, improvement and ultimate recovery are often handicapped, delayed or prevented by an improper diet.

3. The abdomen may remain more or less prominent for several years after apparent recovery, as shown in illustrations.

Early diagnosis was more difficult than when the condition had persisted for months or years. The relative constancy of the age at the

time of onset was a valuable aid; in twenty-one patients, the onset began during the second year of life; in three of the other four, early in the third year. The three cardinal signs present in every instance were, in the order of their severity, prominence and persistence:

1. A prominent, more or less doughy abdomen, relatively free from tympanitis. The circumference of the abdomen in the level of the navel (child preferably in standing position) was invariably greater than the circumference of the chest in the level of the mamillae. Fluoroscopic examination seldom revealed a great excess of gas, as the distention was usually caused by fecal matter in the intestine. The colon was found exceptionally dilated in four instances (table 2, cases 2, 4, 8 and 18).

Figure 4

Figure 5

Fig. 4 (case 8).—Jean H., aged 2¾ years; weight 20 pounds and 4 ounces (9.1 Kg.).

Fig. 5 (case 8).—Jean H., taken fifty days later; weight, 28 pounds 10 ounces (13 Kg.); gain 128 ounces (3.6 Kg.) on protein milk and Ringer's solution.

2. Voluminous stools, often gray and semisoft. The daily output on successive days was invariably surprisingly large in amount.

3. Loss of weight or stationary weight. This had persisted for months or years without any other discernable cause.

Retarded growth, cessation of walking, anorexia, vomiting, anemia, carpopedal spasm and ascites were present in some instances, but were variable in degree. Differential diagnosis excluded visceral tubercu-

losis, dysentery, and infection by *Tricocephalus dispar,* also the pot-belly of rickets, cretanism and megacolon. As far as could be ascertained, none of these cardinal symptoms was ever present during the first year of life.

The dietary regimen is by far the most important part of treatment. Improvement and cure in the mild type require many months; in the

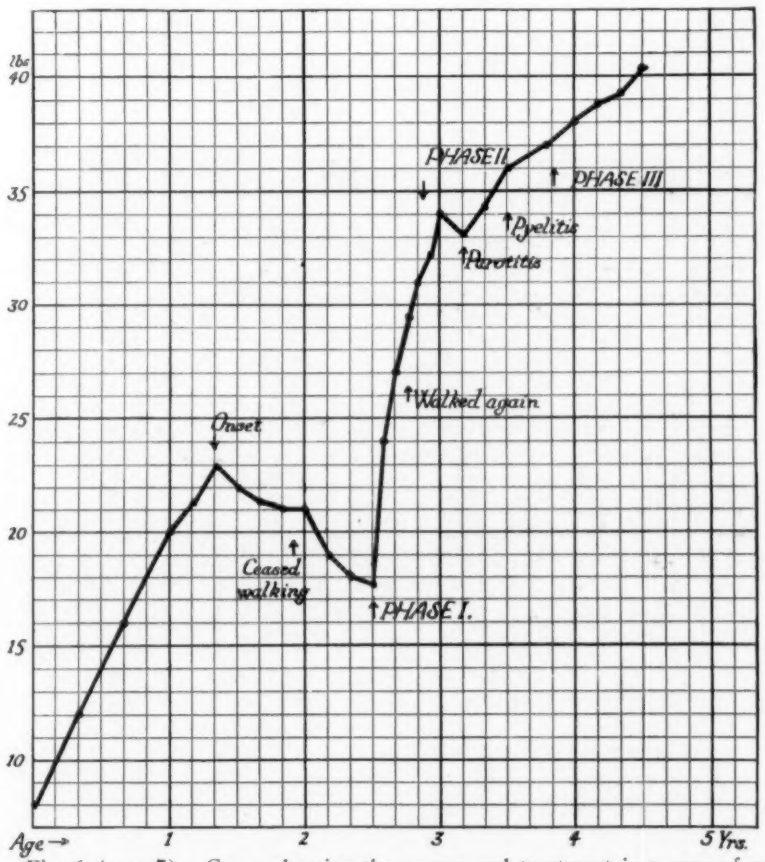

Fig. 6 (case 7).—Curve showing the course and treatment in a case of celiac disease (Jane M.); gained 6 pounds 4 ounces (2.8 Kg.) in first month of diet; 15 pounds (6.8 Kg.) in first six months.

severe type, from one to two years of accurately planned diets, diligent nursing care and an early appreciation of such unfavorable symptoms as vomiting, anorexia, return of abdominal distention, voluminous stools or stationary weight. The experience which most of these mothers acquire, at times before the proper diagnosis and treatment are established, makes them exceptionally cooperative and extremely efficient.

Not infrequently various kinds of foods had been tried and numerous physicians consulted. The chronicity of the ailment, risk of long hospitalization and the susceptibility to intercurrent diseases make an isolated, sunny room at home the ideal place to institute treatment. Hospital

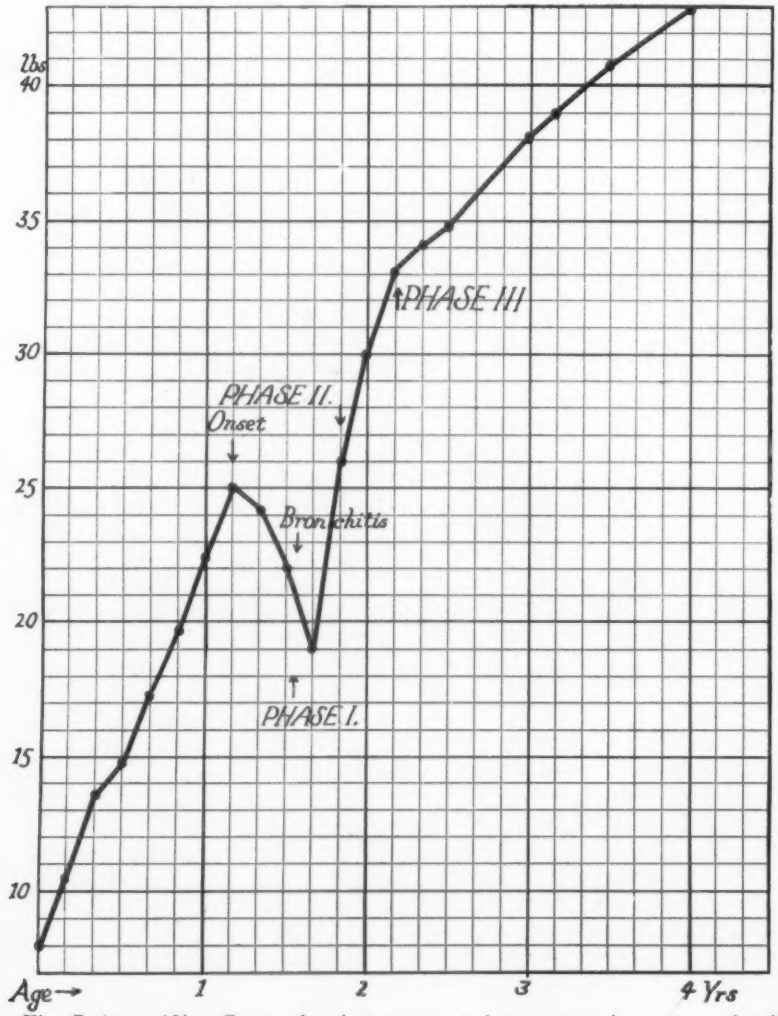

Fig. 7 (case 10).—Curve showing course and treatment in a case of celiac disease (Stephen G.); anorexia and chronic bronchitis present the first two months of diet; gained 7 pounds (3.2 Kg.) in two months.

care or trained help is necessary only in exceptional instances (in cases characterized by extreme anorexia, persistent vomiting, inadequate facilities or poor cooperation). Ample data have been collected from

which simple, standard diets have been formulated for the treatment and cure of patients with the severe and mild types of this chronic intestinal disease.

PROCEDURE

Powdered protein milk diluted with water or Ringer's solution was found to be more efficacious than Finkelstein's standard strength Eiweissmilch as used by Howland, because the consistency and volume of a feeding could be readily adapted to the individual requirements without delay or waste of food. During the trying periods of anorexia and vomiting, so frequently encountered during the first few weeks of any treatment, ample calories could often be supplied by mixing the required number of level, packed tablespoonfuls of any standard commercial powdered protein milk with enough water (sweetened with saccharin)

Fig. 8 (case 10).—Stephen G., aged 3½ years; weight, 40 pounds (18.1 Kg.); abdomen still somewhat prominent.

to form a smooth, palatable paste of cream-like consistency. In a few instances (table 2, cases 12 and 25), the vomiting and anorexia were persistent and powdered skimmed milk was temporarily used to advantage. The level, packed tablespoonful served as the measure of choice, not only because it was found convenient and practical but primarily because the number of level, packed tablespoonfuls required daily usually approximated the number of pounds the child should weigh. This simple, accurate measure made it possible to prepare a feeding within a few minutes before it was served, and the attendant had more time for other duties or relaxation.

STANDARDIZATION OF THREE-PHASED DIET

PHASE 1 *(Protein Milk Alone).*—Howland found that the duration of this phase of the diet depended on the intestinal reaction and somewhat on the age of the child, but he seldom found it necessary to continue it longer than a

few weeks. It is prudent that it be continued until the stools are firm, the distention slight, the gas not in excess and the appetite good. If anorexia and vomiting are absent and if ample food is consumed, the improvement and increase in weight are often so rapid (see charts) that no addition is needed until the child's weight exceeds the best weight before the illness began; by taking this precaution, the tolerance improves most rapidly and exacerbations are least likely to occur. The initial anorexia usually disappears within a fortnight. It is advisable to begin with several level tablespoonfuls of powdered protein milk less than the number of pounds the child weighs. If anorexia is not extreme, four feedings should be given daily. When the child takes the food well,

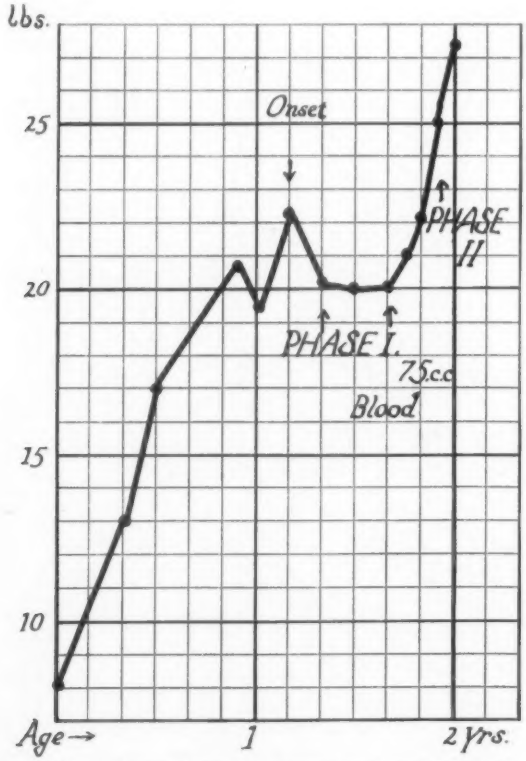

Fig. 9 (case 11).—Curve showing course and treatment in a case of celiac disease (Robert S.); extreme anorexia was present for six months; various diets tried from fourteenth to twentieth month; marked improvement after transfusion.

the number of tablespoonfuls should be increased by two every five to seven days until the number approximates the child's best previous weight. Appetite, vomiting, age, degree of emaciation, season of the year and the presence of complications are factors which should influence the rate of increase. The amount of water or Ringer's solution added to a feeding may be varied to suit the whim of the individual child. Some will take the food best from the bottle, others prefer to drink from a cup, and older children often relish the thick, sweetened food from a spoon. An illustrative case may simplify this explanation of the procedure:

A child, aged 2 years, weighing 16 pounds (7.3 Kg.), has been ill for six months. The best previous weight was 24 pounds (10.9 Kg.). For the twenty-four hour formula use: powdered protein milk 12 (14, 16, 18, 20, 22, 24) level packed tablespoonfuls; Ringer's solution, 24 ounces (710 cc.) more or less; saccharin, 1 grain (0.06 Gm.). Rub the powder with a small quantity of the warm, sweetened Ringer's solution to make a smooth paste; gradually add the remainder of the solution, mix and rub through a fine wire sieve; divide into four portions and place in refrigerator. Heat before serving at 7 and 10 a. m., 2 and 6 p. m. (or at 6 a. m.; noon and night). Water may be used at first instead of Ringer's solution if anorexia is extreme. To prepare an individual

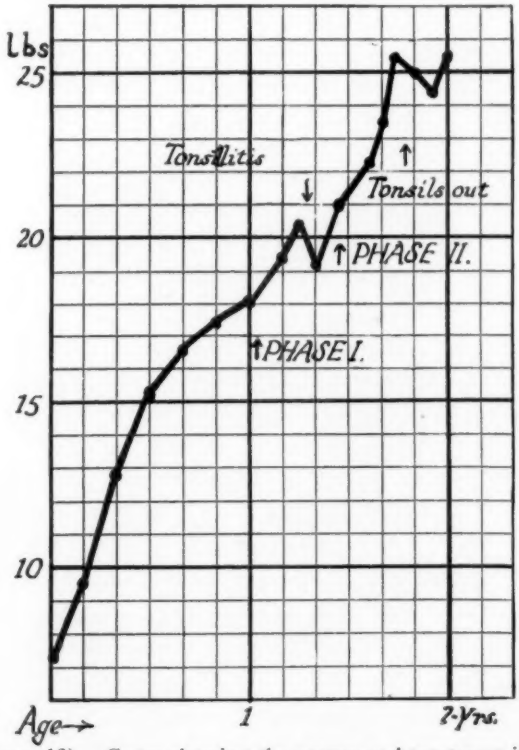

Fig. 10 (case 12).—Curve showing the course and treatment in a case of celiac disease (Romaine S.); owing to persistent anorexia and vomiting diet was changed to powdered skimmed milk at 22 months.

feeding, use a fourth of the foregoing proportions. Ample water should be given between feedings to total a quart or more of fluids in twenty-four hours.

PHASE 2.—When the weight approximates the best weight before the illness began, the Ringer's solution may be discontinued, but the protein milk formula need not be changed for weeks or months. The following additions may be allowed at the 10 a. m. and 6 p. m. feedings: small but increasing quantities of curd without whey, lean beef juice, cottage cheese, scraped beef and egg. If the gain has been satisfactory or if the child dislikes protein milk, an equivalent amount of powdered skimmed milk may be substituted for part of the powdered

protein milk. The addition in weight should continue, and the distention should not increase. Cod liver oil, orange juice and iron should also be given in gradually increasing quantities. The number of tablespoonfuls of protein milk may be increased from month to month as the child's weight progresses. When the weight exceeds 25 pounds (11.3 Kg.), the three meal (7 a. m., noon, 6 p. m.) diet is usually more satisfatory. The duration of this stage is, as Howland says, "many months, it may be years." During this period the child usually continues to increase in weight and grows rapidly. The small amount of sugar in the protein milk and the large quantity of carbohydrate available from the protein guards against acidosis and insures satisfactory development.

PHASE 3 *(Addition of Carbohydrates).*—Well cooked meats (lean beef, mutton, chicken, fish, tongue) are well tolerated if finely minced. Corn syrup, well cooked cereals (rice, farina, arrow root), zwieback and well cooked vegetables

Fig. 11 (case 3).—Dorothy J., aged 7 years; weight, 54 pounds (24.5 Kg.); abdomen somewhat prominent but circumference less than chest. This is the oldest child in the series.

may be cautiously added in slowly increasing amounts. Bread, potato, sugar, ice-cream, candy, cake and fresh milk should never be added within the first year, preferably not until the end of the second year of treatment. Should parenteral infections, hot weather, overfeeding or premature additions to the diet precipitate an exacerbation, then phase 1 should be resumed without delay.

CONCLUSIONS

1. The celiac syndrome disappears when fresh cow's milk, carbohydrate and fats are omitted.

2. Their premature addition or inclusion is likely to provoke an exacerbation.

3. Noxious intestinal products, probably formed by bacterial action on these foods, play an important rôle in etiology.

4. This disease has never been produced experimentally, but circumstantial evidence leads to the hypothesis that it might be transmitted from one child to another.

5. Prognosis depends on the diet rather than on the severity or duration of the disease.

6. A standard, three-phased, high protein diet yielded rapid and permanent results in a majority of the twenty-five patients for whom it has been prescribed during the past seven years.

THE INTRADERMAL SALINE TEST IN SERUM SICKNESS *

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When physiologic sodium chloride is injected into the skin of a normal person, it produces a distinct, elevated blanched area, from 1 to 1.5 cm. in diameter, at the point of injection. The hair follicles are distinctly visible on the center of this area. As the saline solution is absorbed, this elevation becomes less palpable; it finally disappears in about sixty minutes in adults and somewhat more quickly (from thirty to fifty minutes) in infants.

It was found by McClure and Aldrich [1] that the disappearance time was much diminished in a group of children with edema as compared with that in a group of control cases; furthermore, that the greater the degree of edema, the shorter the disappearance time and vice versa. The authors showed that by the use of the test, the occurrence of edema might be foretold before it was demonstrable clinically. Moreover, they found that an increase in the disappearance time preceded a diminution in the edema in certain cases. They concluded, therefore, that the test had a certain immediate prognostic value in nephritis with generalized edema.

Baker,[2] who used the test in seventy cases of scarlet fever and in thirty cases of diphtheria, principally in children, found in these a reduction of the disappearance time, with a close correlation between the shortening of the time and the severity of the intoxication.

Harrison [3] applied the same test in cases of lobar pneumonia in children between the ages of 2 and 14 years, and he concluded that there was a marked shortening of the disappearance time of intradermally injected salt solution, and that the crisis had no immediate effect on the length of the disappearance time. After the crisis, the return to normal was usually slow.

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* From the Department of Pediatrics, The University of Rochester and The Pediatric Service of the Strong Memorial Hospital.

1. McClure, W. B., and Aldrich, C. A.: Time Required for the Disappearance of Intradermally Injected Salt Solution, J. A. M. A. **81**:293 (July 28) 1923. Aldrich, C. A., and McClure, W. B.: The Intradermal Salt Solution Test, J. A. M. A. **82**:1425 (May 3) 1924.

2. Baker, W. J.: Intradermal Salt Solution Test in Scarlet Fever and Diphtheria Patients, J. A. M. A. **83**:1561 (Nov. 15) 1924.

3. Harrison, J.: Intradermal Salt Solution Test in Lobar Pneumonia in Children, J. A. M. A. **84**:1258 (April 25) 1925.

Stern and Cohen [4] made use of the test as a method of determining circulatory deficiencies of extremities in the absence of edema. They found it of considerable practical value in certain surgical conditions due to impaired circulation, as gangrene.

Olmsted [5] found a shortened disappearance time in cardiac disease. Lash [6] reported definite shortening of this time in the toxemias of pregnancy; and Lovett,[7] while recently applying the test to patients with scarlet fever, observed three cases of urticaria due to serum which were associated with a diminished disappearance time.

Because of the unusually frequent occurrence of serum sickness following the administration of certain brands of diphtheria antitoxin and of antistreptococcic scarlet fever serum, it seemed of interest to apply the test in this condition in which there is evidently some disturbance in the fluid balance of the tissues.

The technic used was the same as that employed originally by McClure and Aldrich. With a 1 cc. Luer tuberculin syringe and a 26 gage hypodermic needle, 0.2 cc. of sterile physiologic sodium chloride was injected into the skin, usually on the flexor surface of the forearm near the elbow. The persistence of the elevation thus produced was determined by palpation of the area, and the duration in minutes was carefully noted.

Tests were applied in eighteen cases of serum sickness. Rapid absorption of the saline solution was noted in each case. In eight cases, tests were made when the patients were admitted to the hospital and were repeated during the course of serum sickness. In certain instances, the percentage of serum protein and the surface tension of the blood serum were determined, because Clausen [8] has shown that both the serum protein and the surface tension are markedly lowered in the edema of nephrosis, in which there is generalized disturbance of equilibrium between the tissues and the body fluids. The determinations of serum protein were made by the refractometric method, and the surface tension was measured by means of the du Noüy apparatus. In a few instances, the serum chlorides were also determined.

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4. Stern, W. G., and Cohen, M. B.: Intracutaneous Salt Solution Wheal Test, J. A. M. A. **87**:1355 (Oct. 23) 1926.

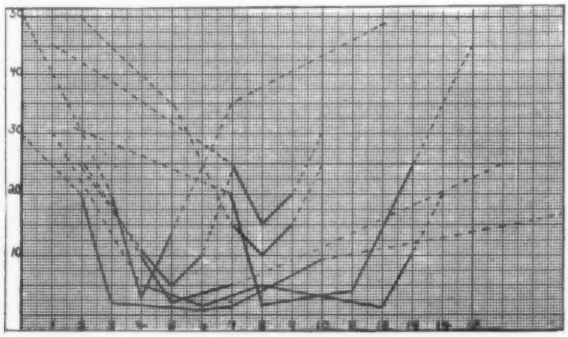
5. Olmsted, H. C.: Intradermal Salt Solution Test in Cardiac Disease in Children, Arch. Int. Med. **37**:281 (Feb.) 1926.

6. Lash, A. F.: Intradermal Salt Solution Test in Normal and Toxemic Pregnancies, Surg. Gynec. Obst. **43**:40 (July) 1926.

7. Lovett, Beatrice: The Intradermal Salt Solution Test in Scarlet Fever, Am. J. M. Sc. **173**:539 (April) 1927.

8. Clausen, S. W.: Parenchymatous Nephritis: III. The Surface Tension of the Blood Serum, Am. J. Dis. Child. **29**:581 (May) 1925.

Tables 1 and 2 show the typical observations made in a few cases studied. The accompanying illustration shows the curves obtained in eight cases of serum sickness. It will be noted that the disappearance time is shortest when the serum sickness is most pronounced. In each case, there is a marked decrease in the time as serum sickness occurs and a return toward normal as it subsides. Table 1 gives the disappearance time, serum protein and surface tension in ten control cases. Table 2 illustrates the same determinations in relation to the disappearance time and to the time of administration of serum in eight cases of serum sickness; chloride values are given in six of these cases.



The ordinate indicates the disappearance time in minutes of the elevated, blanched area which appears after the injection of physiologic sodium chloride; the abscissa, the time in days after the administration of serum; the solid lines, the duration of the serum sickness.

TABLE 1.—*Observations Made on Ten Control Cases*

Name	Age	D. T.	S. P.	S. T.	Diagnosis
H. K.	11	60	7.2	60	Diphtheria carrier
F. G.	12	45	7.6	63	Diphtheria carrier
G. J.	13	65	6.7	61.5	Diphtheria carrier
C. B.	14	55	7.4	61	Diphtheria carrier
M. G.	2 mos.	35	5.4	58	Normal infant
S. P.	7	55	7.2	62	Perthe's disease
M. V.	11	60	8.2	62	Sydenham's chorea
J. D.	4 mos.	30	6.7	55	Prematurity
C. L.	14 mos.	35	7.3	59	Diabetes
H. C.	6	55	8.7	60	Epilepsy

D. T. indicates the disappearance time in minutes; S. P., serum protein percentage; S. T., the surface tension in dynes per centimeter.

The formation of wheals in various conditions has been the subject of considerable study. By using a 1 : 1,000 solution of codeine as a wheal-producing agent, Pilcher [9] studied the production of wheals in

9. Pilcher, J. D.: Wheal Formation in Infants and in Children, Am. J. Dis. Child. **31**:77 (Jan.) 1926.

edema due to various causes. In a case of serum urticaria, he noted that the codeine wheal and the serum wheal were much alike, and that the serum wheal was little changed by the additional stimulation of codeine. He suggested that the two substances probably acted on the same vascular structures. The same author, working with Sollman,[10] previously had studied the production of wheals by various drugs, and had concluded that the probable mechanism in the production of urticaria was a specifically increased permeability of the capillaries or lymph vessels.

CONCLUSIONS

From these observations, it would seem that there is a definitely increased avidity of the tissues for water in serum sickness. This is

TABLE 2.—*Clinical Data of Eight Patients with Serum Sickness*

Name and Age	D. T.	S. P.	S. T.	S. Chl.	T. A. S.	Comment
M. S., 4, diphtheria....	6	7.42	63	...	10	Urticaria fading
	25	7.85	63	...	12	No edema
	45	6.98	63	...	14	Urine normal
H. B., 4, diphtheria....	20	6.98	61	...	2	Localized urticaria urine negative
	2	7.42	61	...	6	Severe serum rash—edema
	8	6.55	61.6	...	11	Joint envolvement
F. L., 9, scarlet fever...	5	7.42	63	574	4	First day of serum sickness
	3	6.55	63	559	6	Extensive rash with edema
	6	6.92	61.6	477	7	No rash—edema
	20	8.16	59	535	13	No evidence of serum sickness
E. B., 14, scarlet fever..	2	7.63	65	550	5	First day of urticaria
	25	8.16	61.6	558	16	Urine negative, no complications
F. D., 13, scarlet fever..	50	7.09	63.7	524	2	No evidence of serum sickness
	25	6.55	62.3	535	9	Two days after moderate rash
M. B., 4, diphtheria.....	25	6.98	61.6	538	2	Three days before urticaria
	5	6.98	60.9	470	5	First day of rash
R. W., 4, diphtheria.....	15	6.87	58.1	547	8	Generalized serum eruption
	30	6.98	60	530	10	Rash gone—urine negative
R. S., 8, scarlet fever...	2	7.09	61	595	14	Severe serum sickness—generalized edema—acute urinary retention

D. T. indicates the disappearance time in minutes; S. P., the serum protein percentage; S. T., surface tension of the blood serum in dynes; S. Chl., serum chlorides mg. per hundred cubic centimeter; T. A. S., time after serum administration in days.

greatest when the eruption is most intense and in cases in which edema or involvement of the joints is most extensive. The disappearance time may be shortened even after the rash has disappeared, but it gradually returns to normal. In comparing the duration of serum sickness to the initial salt test, it is suggested that a long duration is usually associated with a short initial disappearance time, and conversely, that a long initial disappearance time is associated with a brief duration of serum sickness. Further observations, however, are necessary to establish this relationship, because both the age and the presence of scarlet fever or diphtheritic infection modify the disappearance time.

10. Sollman, T., and Pilcher, J. D.: Endermic Reactions, J. Pharmacol. & Exper. Therap. **9**:307 (March) 1917.

In serum sickness, there is a retention of chlorides and of water frequently associated with albuminuria and occasionally with impairment of renal function. According to Longcope and Rackemann,[11] this retention of salt and of water takes place primarily in the tissues rather than in the blood. Changes in the serum chlorides, in the serum protein and in the surface tension of the serum did not occur in the group of cases studied. The mechanism, therefore, differs from that in nephrosis.

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11. Rackemann, F. M.; Longcope, W. T., and Peters, J. P.: The Excretion of Chlorides and of Water and the Renal Function in Serum Sickness, Arch. Int. Med. **18**:496 (Oct.) 1916.

RICKETS IN THE NEGRO

EFFECT OF TREATMENT WITH ULTRAVIOLET RAYS *

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The use of the ultraviolet rays in the treatment of patients with rickets is of great interest at present, especially since their mode of action is being clarified. No one doubts that these rays cure rickets. Hess,[1] Steenbock, Orr [2] and many others have shown that cures are obtained by the use of this agent alone. A conclusive investigation of the effect of ultraviolet rays on rickets in the negro [3] has not, however, been carried out, in spite of his marked susceptibility to the disease. Park J. White,[4] in a comparison of the incidence of rickets and malnutrition among infants in a clinic, has shown that both these conditions occur three times as frequently in colored infants as in white. This confirms the generally accepted opinion.

In a fairly careful search of the literature, particularly of southern medical journals, I have been unable to find a satisfactory explanation for this increased incidence of rickets in the colored race. Sambon,[5] as far back as 1907, showed that when light was passed through pigmented skin, the ultraviolet or short waves were filtered out in direct proportion to the density of the pigmentation. It is likely that this observation has been the innocent cause for misunderstanding. Thus, Hess and Unger,[6] in 1917, quoting Sambon's observation stated:

> It seems probable that the exceptional incidence of rickets among negro infants in New York and other northern cities is attributable in part, to the pigmentation of their skins, which, as is well known, prevents the penetration of the short actinic rays.

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* Received for publication, July 9, 1927.

* From the Pediatric Service of the Barnert Memorial Hospital, Paterson, N. J.

1. Hess, Alfred F.: The Rôle of Ultraviolet Rays in Rickets, Atlantic M. J. **27**:467, 1923.

2. Orr; Holt; Wilkins, and Bonne: The Ca and P Metabolism in Rickets with Special Reference to Ultraviolet Ray Therapy, Am. J. Dis. Child. **26**:362 (Oct.) 1923.

3. DeBuys, L. R.: Personal communication to the author.

4. White, Park J.: Abstract of Report on the Health of Colored Babies in St. Louis, Am. J. Dis. Child. **28**:262 (Aug.) 1924.

5. Sambon, L. W.: J. Trop. Med., Feb. 15, 1907.

6. Hess and Unger: Interpretation of Seasonal Variation of Rickets, Am. J. Dis. Child. **22**:186 (Aug.) 1921.

On the other hand, it is known that rickets is not common among negroes in the tropics. Ker, of Jamaica, B. W. I., Pierce of Panama, Scheult of Trinidad and others, in personal communications to Hess,[7] have stated that rickets is exceedingly rare among negroes in these localities. The difference may be a quantitative one, depending on the greater amount and intensity of sunlight available in the tropics.

Hess, Unger and Jarecky [7] have shown that the diet in the ordinary northern negro community is markedly deficient in fresh vegetables and fruits, and that the food is cooked too long. This may also be a definite factor in the increased incidence of rickets in northern negroes, and may explain the rarity of this condition among negroes living in the tropics, where the diet consists for the most part of fresh fruits and vegetables.

Schultzer and Sonne,[8] investigating the prophylactic action of light in experimental rickets, showed that protection was less effectual in black than in lighter colored rats.

Lesné and de Gennes,[9] referring to this work of Schultzer and Sonne,[8] stated that they had been able to confirm clinically these experiments. They reported two cases of rickets in colored children whom they treated by twenty-four exposures to ultraviolet rays; each exposure was of more than thirty minutes' duration. This treatment did not have any influence on the clinical signs or rachitic stigmas.

These observations have probably helped to create the prevailing impression that light therapy is ineffective in the treatment of rickets in negroes. Contrary observations made by the physicians in the tropics led me to try this form of therapy in an advanced case of rickets in a negro.

REPORT OF A CASE

J. H., a negro boy, aged 2, weighing 20 pounds, 1 ounce (9 Kg.), was admitted to the hospital on March 14, 1927, because of inability to walk. The family history was negative. The patient had been a full term, normal child, breast fed until 9 months of age when he was given a mixed diet. He had not had any of the illnesses of childhood except "colds," and he had not had convulsions. He sat up at 4 months, the first teeth erupted at 9 months, and he started to talk at 15 months. He had never been able to walk.

Three weeks before admission, the mother started to give the child cod liver oil, but definite amounts were not administered, nor was it given regularly.

Physical examination, on admission, showed a full-blooded, negro infant, undersized and poorly nourished, who appeared bright and happy, but who was unable to stand or walk unsupported. The head was large, the anterior fontanel

7. Hess, Unger and Jarecky: The Diet of the Negro Mother in New York City, J. A. M. A. **70**:900 (March 30) 1918.

8. Schultzer, P., and Sonne, C.: Prophylactic Action of Light in Experimental Rickets, Hospitalstid. **66**:541 (Aug. 1) 1923.

9. Lesné, E., and de Gennes, L.: Le traitement du rachitisme par les rayons ultra-violet, J. méd. franç., 1925, vol. 14.

Fig. 1.—J. H., negro infant with "pot-belly," umbilical hernia, epiphyseal enlargement and bowed legs.

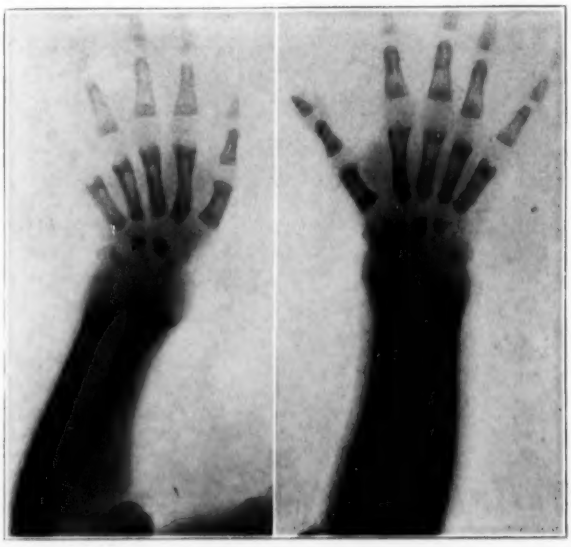

Fig. 2.—Condition in negro infant on admission and before treatment was started; "fraying," brushlike appearance and "cupping" are characteristic of rickets.

was slightly open; there was no evidence of craniotabes. The abdomen was markedly protuberant; lordosis and umbilical hernia were present. The wrists showed epiphyseal enlargement, and a rachitic rosary could be felt over the ribs; there was marked bowing of the tibiae, and pes planus was present. The patient had two lower and four upper central incisors:

The child was placed on a mixed diet of milk, bread, cereals, fruits and vegetables. Cod liver oil was not administered, and egg-yolk was not allowed. This was in accordance with the observations of Hess,[10] and Casparis, Shipley and Kramer [11] that egg-yolk exerts a definitely antirachitic influence.

Figure 2 shows the condition present one week after admission, just before treatment was started. It is exactly the same as that noted on admission, and shows a widened and irregular outline at the preparatory zone of calcification, with "fraying" of the edges, brushlike appearance, and "cupping" characteristic of rickets.

The patient was treated solely by exposure to ultraviolet rays from a mercury vapor quartz lamp. Treatment was started with three minutes of exposure at a

Data and Result of Treatment in a Case of Rickets in a Negro Infant

Date	Roentgenogram	Blood Calcium Mg. Percentage	Hemoglobin Sahli	Walking	Teeth	Red Cells	Erb's Test	Mantoux	Wassermann Reaction
3/16/27	Florid rickets.....	9.5	76%	—	6	3,480,000	—	—	—
3/22/27	Florid rickets (fig. 2.).	9.5	....	—	6	.....	..	..	..
	Treatment started March 23, 1927.								
3/30/27	No change.....	9.0	70%	—	6	4,000,000	..	..	..
4/9 /27	No change.....	9.0	70%	+	6	3,030,000	..	..	..
4/14/27	Beginning calcification. (fig. 3.).....	10.4	....	+	6	.....	..	..	..
4/22/27	Further calcification..	10.0	....	+	6	.....	..	..	..
5/5 /27	Complete cure (fig. 4.)	12.0	92%	+	8	4,000,000	..	..	..

distance of 30 inches (76.20 cm.), the time being increased one minute daily up to fifteen minutes. The dosage was then continued.

Progress of the case was recorded by weekly roentgen-ray examinations and determinations of blood calcium. The blood calcium rose from 9 mg. per hundred cubic centimeters at the beginning of treatment to 12 mg at the end.[2] The hemoglobin rose from 70 per cent to 92 per cent (Sahli). After two weeks, the child began to walk, and improvement continued until he was discharged. At the end of six weeks, two new teeth were erupting.

The roentgenograms at the end of three weeks (fig. 3) showed definite evidence of calcification at the preparatory zone of calcification, less "fraying" and distinct evidence of healing. After six weeks, the cure was complete (fig. 4).

COMMENT

It appears from the foregoing case that rickets in a negro was cured by ultraviolet rays. The question arises whether there is a quantitative difference in the effect of the rays on white and colored children.[8]

10. Hess: Therapeutic Value of Egg-Yolk in Rickets, J. A. M. A. **81**:15 (July 7) 1923.

11. Casparis, Shepley and Kramer: Antirachitic Influence of Egg-Yolk, J. A. M. A. **1**:818 (Sept. 8) 1923.

Fig. 3.—Roentgenogram showing condition after three weeks of treatment; beginning line of calcification is distinct.

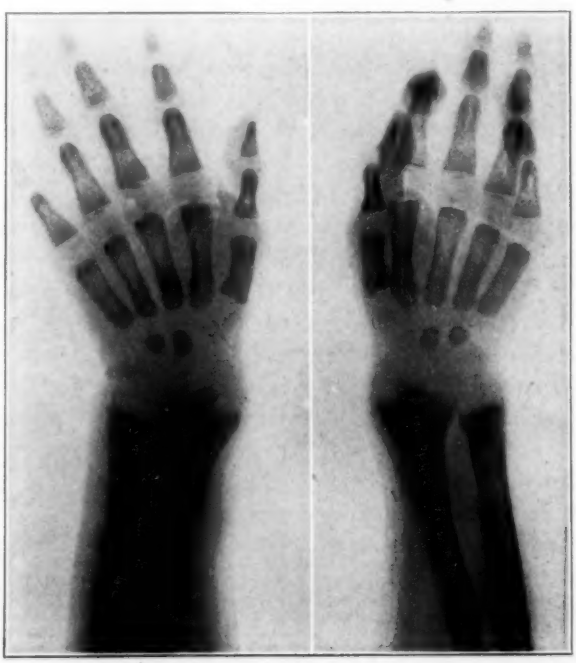

Fig. 4.—Roentgenogram showing condition after six weeks of treatment; large center of ossification; preparatory zone of calcification completely calcified and healed rickets are noted.

Unfortunately, the amount of clinical material in the Barnert Memorial Hospital is too small to permit me to answer to this question. This case is reported with the hope that further investigation may give more conclusive evidence. However, I feel that some deductions can safely be made even from this one case.

From the literature, it appears that the earliest roentgenologic evidence of healing by light therapy is demonstrable at the fourteenth day. The average time is about twenty-one days. The dosage of rays generally used is the same as was employed in this case, i. e., three minutes at 30 inches, increasing one minute daily to fifteen minutes, and continuing at this dosage; in other words, this negro was treated in the standard way, and other antirachitic factors were excluded.

Roentgenograms taken on the twenty-first day showed definite evidence of healing. Therefore, with no more intensive treatment than has been given to thousands of white babies, this colored child showed a healing time which compares favorably with the best results reported in the literature.

From this it seems reasonable to deduce that the pigmented skin of the negro does not appreciably retard the effect of the ultraviolet rays in the treatment of patients who have rickets.

The ultraviolet rays appear to be essential to life, and if they are capable of exerting so powerful a synthetic and metabolic effect as they evidently are, it would be unreasonable to suppose, from a biologic point of view, that nature would provide the colored races with a pigment in the skin sufficient to exclude these vital rays. It would seem more reasonable to seek an explanation for the observation here made that the pigment of the skin does not have a retarding effect on the biologic activity of the rays, and such an explanation may now be offered.

According to the conceptions of Kowarschick [12] and other physiotherapists, the effect of the ultraviolet rays is a systemic one, achieved through the direct absorption of these rays by the blood in the superficial capillaries of the skin. This conception in the light of recent work, however, scarcely seems tenable. Hess,[13] Steenbock [14] and others have shown that activated cholesterol exerts the same antirachitic effect as ultraviolet rays; in other words, any substance containing cholesterol can be rendered antirachitic by exposure to these rays. This is probably the manner in which the quartz lamp works when it is used for the treatment of persons with rickets.

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12. Kowarschick: Personal communication to the author.

13. Hess, Alfred F., and Weinstock, M.: Antirachitic Value of Irradiated Cholesterol and Phytosterol, J. Biol. Chem. **64**:181 (May) 1925.

14. Steenbock, H., and Daniels, A. L.: Irradiated Foods and Irradiated Organic Compounds, J. A. M. A. **84**:1093 (April 11) 1925.

The granules of pigment in the skin are in and between the lowest layers of the epidermal cells, i. e., in the lowest layers of the stratum germinativum,[15] and the epidermal cells superficial to this pigment layer contain cholesterol.[16] The observation of Sambon [5] that the ultraviolet rays are filtered out when light is passed through pigmented skin may therefore be correct, yet the biologic effect of these rays would not be retarded when used for the treatment of negroes with rickets, since they do not have to penetrate the pigment in order to activate the cholesterol in the epidermal cells. This antirachitic cholesterol can be absorbed by the capillaries of the skin to exert its systemic effect.

That ultraviolet rays exert their antirachitic effect by activating the cholesterol of the skin is not a new theory. It has been suggested by various investigators, and Hess and Weinstock [13] have shown that irradiated human skin, when fed to rats, was antirachitic. This theory is mentioned only because it explains adequately the fact that the pigmented skin of negroes does not have a retarding effect on the antirachitic influence of ultraviolet rays.

SUMMARY

A negro infant with an advanced case of rickets was treated by ultraviolet rays. Healing began in three weeks, and the child was cured in six weeks.

Pigmented skin does not appear to have a retarding effect on the curative action of ultraviolet rays in rickets. An explanation is offered.

282 Broadway.

15. Lewis and Stohr: A Text Book of Histology, ed. 2, Philadelphia, P. Blakiston's Son & Company, 1914, p. 384.

16. Eckstein and Wile: The Cholesterol Content of the Cutaneous Epithelium in Man, Proc. of the Am. Soc. Biol. Chemists, 20th Ann. Meeting, Supp. 1 to J. Biol. Chem., Feb., 1926.

TUBERCULOSIS OF THE CERVICAL LYMPH NODES IN INFANCY

VALUE OF THE ROENTGEN RAY IN DIAGNOSIS *

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Calcification of the lymph nodes in children is almost certain evidence that the infection of the nodes is tuberculous. Roentgen-ray examination has proved to be a simple means for demonstrating the presence of calcification in lymph nodes, even though the latter lie in the abdominal cavity. The use of the roentgenogram for the demonstration of calcium in cervical nodes and its importance in differentiating tuberculous from nontuberculous adenitis has been fully described by Hanford,[1] and the characteristics of the shadows cast by abdominal tuberculous nodes have been set forth in a previous paper.[2] Our purpose in this paper is to point out the value of examination by means of the roentgen ray for the diagnosis of tuberculous cervical adenitis in infancy, a period of life in which tuberculosis of these nodes is regarded as rare.

TECHNIC

The technic used in taking roentgenograms of the neck is simple. The patient lies on the back with chin raised and neck extended. The plate used to take the roentgenogram of the chest in children can easily be placed so as to include the neck also. If nodes can be felt high in the neck, it may be best to turn the head slightly so as to avoid the shadow of the mandible and thus expose the whole chain of nodes reaching from the styloid process to the clavicle. The anteroposterior view has been found most satisfactory. Though lateral roentgenograms may show the nodes, they are often unsatisfactory, because the shadows of the nodes are apt to be superimposed on the shadows of the spine, skull or mandible.

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* From the Pediatric Department, Yale University School of Medicine.

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1. Hanford, J. M.: The Roentgen-Ray Diagnosis of Tuberculous Lymph Glands, Am. J. M. Sc. **164**:539 (Oct.) 1922.

2. Dunham, E. C., and Smythe, A. M.: Tuberculosis of Abdominal Lymph Nodes: Diagnosis by Means of the Roentgen Ray, Am. J. Dis. Child. **31**:815 (June) 1926.

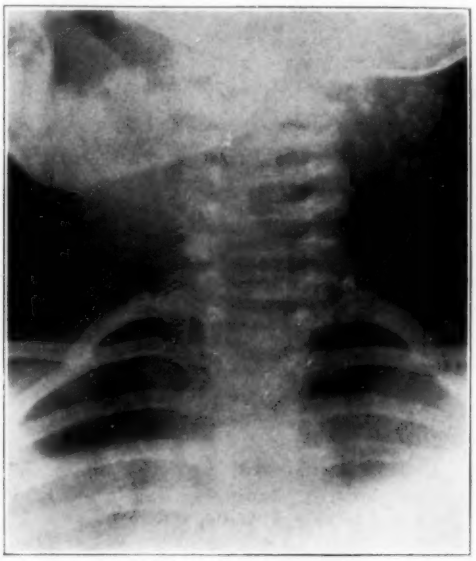

Fig. 1 (case 1).—Roentgenogram of the neck of an infant, aged 9 months. The calcified areas on the left side are visible in a plate taken when the infant was 5 months old; that plate, unfortunately, is unsatisfactory for reproduction.

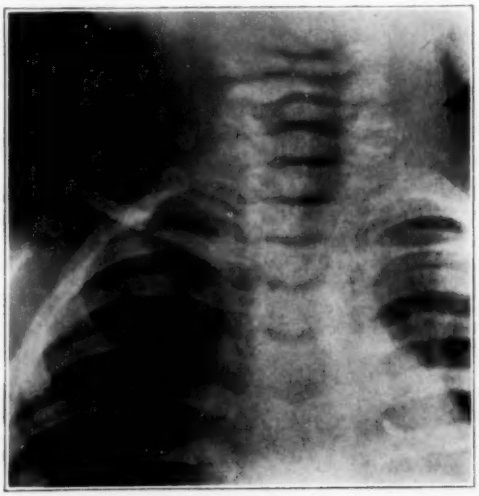

Fig. 2 (case 2).—Roentgenogram of neck of an infant, aged 1 year.

REPORT OF CASES

In the course of routine examination of children in the tuberculosis clinic of the New Haven Dispensary, calcification of cervical lymph nodes was found in several instances. In two infants a diagnosis of tuberculous cervical adenitis was made possible by means of the roentgen ray. In one case calcification was demonstrated when the infant was only 5 months old.

CASE 1.—C. K. was first seen at the age of 5 months with a history of otitis media and cervical adenitis which had been present for about four months. Physical examination revealed chronic suppurative otitis media on the left side with enlargement of the posterior cervical and posterior and anterior auricular nodes on that side. The tuberculin test was positive (0.1 mg. of O.T. tuberculin). At this time roentgenograms of the lungs showed nothing abnormal. An adenoidectomy was performed, followed in a month by a mastoidectomy. Four months later, because the cervical adenitis and otitis media persisted, a roentgenogram of the neck was taken which showed a chain of calcified nodes on the left side (fig. 1). Roentgenograms of the lungs and abdomen still showed nothing abnormal. Reexamination, however, of the roentgenogram of the chest taken when the child was 5 months old—the roentgenogram happened to include the neck—showed calcification of the nodes on the left side of the neck which had not previously been noticed.

CASE 2.—M. P. was 7 months of age when first seen. Physical examination showed bilateral otitis media, enlarged tonsils, furunculosis of the scalp and small "shotty" lymph nodes in the neck. The tuberculin test was positive. Roentgenograms were not taken at this time. Five months later, when the patient was 1 year old, the cervical nodes were "slightly enlarged and shotty," and a roentgenogram at this time showed two small areas of calcification on the right side of the neck (fig. 2). Roentgenograms of the lungs and abdomen showed nothing abnormal. The tonsils and adenoids were then removed. Roentgenograms taken when the child was 18 months old (March, 1927) showed the shadows in the neck unchanged. Roentgenograms of the abdomen taken at this time disclosed calcified nodes on the left side at the level of the third lumbar vertebra. This case is of particular interest because the enlargement of the nodes was neither sufficient nor of such a nature as to make possible the diagnosis of tuberculosis. The discovery of calcification in the nodes on roentgen-ray examination came as a surprise.

Both case reports are of interest because the demonstration of calcification in the lymph nodes of the neck by means of the roentgen ray made the diagnosis of tuberculous infection of these nodes certain at so early an age, in one case at 5 months. Both infants described in the reports are living and well at the ages of 3½ years and 22 months, respectively. The local condition in the neck remains unchanged in both instances.

CONGENITAL HEART BLOCK

REPORT OF A CASE *

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The fifteen cases of congenital heart block previously described have been summarized and presented by Carter and Howland,[1] by Romberg and White [2] and by Wilson and Grant. [3] A tabular survey of symptoms and signs appears in the first of these articles. The case reported by Wilson and Grant is unique in that it is accompanied by a careful postmortem study of the heart, with particular attention to the conduction system.

An additional case of complete heart block associated with congenital malformation of the heart is presented herewith.

History.—Charlotte S. was admitted to the Babies' Hospital, June 5, 1926, at 7 months of age. The parents and a brother, aged 2, were alive and well; the mother had had no miscarriages or stillbirths. The patient, who weighed 7½ pounds (3.4 Kg.) at birth, was born at term after a normal labor of four hours' duration. When delivered, both hands and forearms were reported to be pale and bloodless, but cyanosis was not observed. She was nursed for three months, gained rapidly and appeared to be doing well in every way. At the age of 3 months she developed pneumonia, which was said to have been followed by measles. It became necessary to wean her, and considerable difficulty was experienced with the feeding problem. She suffered from persistent cough, was restless and slept poorly. Since her recovery from the measles she had had a punctate eruption over the entire body. In the five days before admission she had fever ranging from 100 to 103 F.; she lost her appetite and vomited occasionally.

Examination.—On admission her temperature was 95 F. She weighed 3,520 Gm. (7 pounds, 11½ ounces) and measured 60 cm. (23½ inches) in length; the circumference of the head was 37.5 cm. (14¾ inches) and of chest 33 cm. (13 inches). She was poorly developed and undernourished and was weak and fretful. There was a sudaminal eruption on the trunk. She was pale, but free from cyanosis. The cervical, axillary and inguinal lymph glands were easily palpable. The anterior fontanel was level and admitted two fingers. There

* Received for publication, July 30, 1927.

* From the Department of Diseases of Children, College of Physicians and Surgeons, Columbia University and the Babies' Hospital.

1. Carter, E. P., and Howland, J.: Occurrence of Congenital Atrioventricular Dissociation; Report of Case of Congenital Complete Heart Block, Bull. Johns Hopkins Hosp. **31**:351 (Oct.) 1920.

2. Romberg, E. C., and White, P. D.: Congenital Heart Block, Boston M. & S. J. **190**:591 (April 3) 1924.

3. Wilson, J. G., and Grant, R. T.: Congenital Malformation of Heart in Infant Associated with Partial Heart Block, Heart **12**:295 (March) 1926.

was no craniotabes; eyes, ears and nose were normal. She did not have any teeth. The buccal mucous membrane showed good color. The chest was symmetrical, there was no rosary, and the pulmonary areas were normal to percussion and auscultation. The area of cardiac dulness extended from the midline to a point 1.5 cm. beyond the left nipple line. The point of maximum

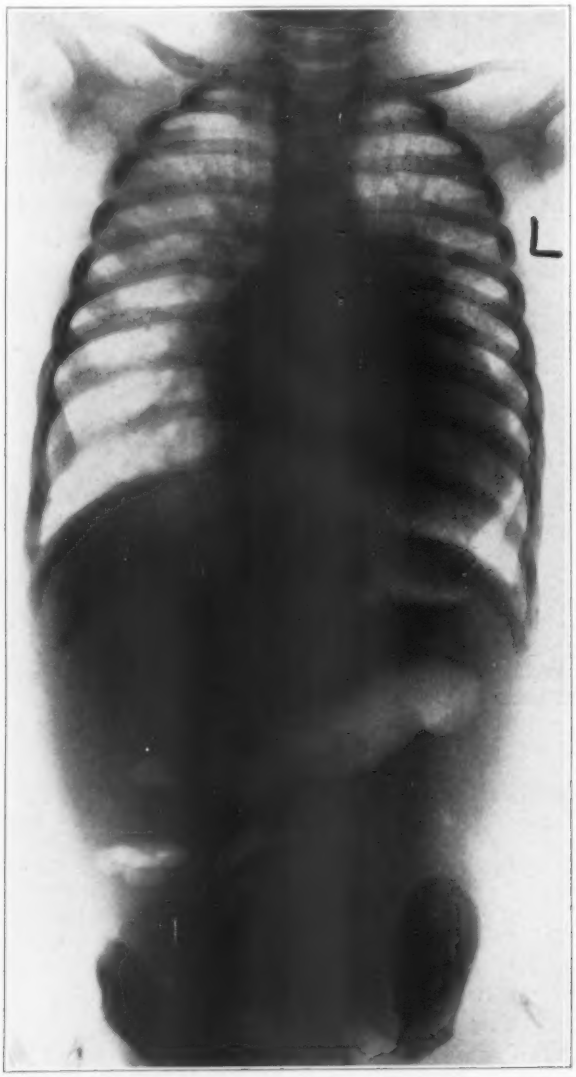

Fig. 1.—Roentgenographic appearance of heart; distance of tube, 6 feet.

impulse was located 1 cm. lateral to the left nipple line in the fourth intercostal space. A thrill could not be felt. The heart rate was slow, from 60 to 64, but the rhythm was regular, and the rate appeared to be independent of bodily activity. A prolonged systolic murmur was audible all over the chest, but was

loudest at the apex. The radial pulses were equal and easily obtained. The abdomen was soft. The edge of the liver was palpable 2 cm. below the costal margin; the tip of the spleen was just palpable. Hernia was not present, and the reflexes were normal. There was no clubbing of fingers or toes.

Urinalysis was negative. The blood count showed: hemoglobin, 60 per cent (Dare); erythrocytes, 3,600,000; leukocytes, 12,850; polymorphonuclears, 73 per cent; platelets, 152,000; the stained smear was negative The throat culture for diphtheria bacilli was negative, and the vaginal smear for gonococcus was negative. The intradermal tuberculin test was negative (0.1 mg.) as were also the blood Wassermann and Kahn tests. The spinal fluid was under normal pressure, clear and free from globulin; the sugar content was 69 mg. in 100 cc.; chlorides, 688 mg. in 100 cc.

Report of a roentgen-ray examination of the chest, June 8, 1926, was as follows: "The heart shadow is large and globular. The lungs suggest a

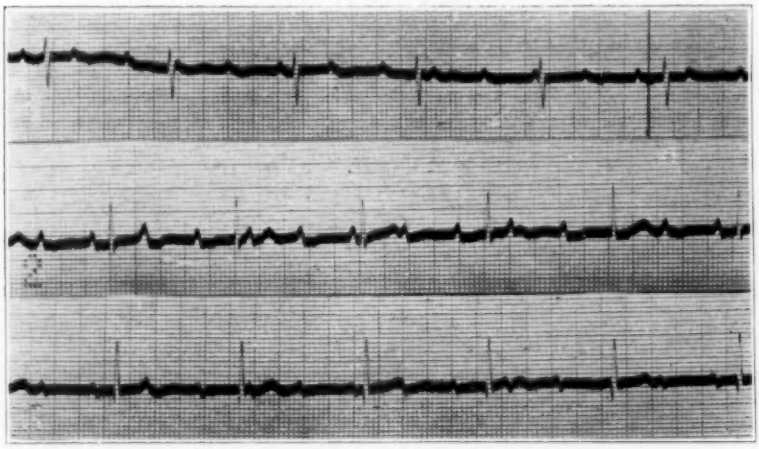

Fig. 2.—Electrocardiogram of complete heart block; leads 1, 2 and 3.

bronchopneumonia, with small hazy areas throughout both upper lobes, but evidence of liquid is not present."

Treatment and Course of Illness.—Atropine sulphate, $\frac{1}{500}$ grain (0.00013 Gm.), was given every four hours for two days, with resulting capillary flush and thirst, but without effect on the heart rate. An electrocardiogram, made at the Presbyterian Hospital on June 12, through the kindness of Dr. R. L. Levy, showed "complete heart block; auricular rate, 135; ventricular rate, 57; right preponderance and T waves upright in all leads. This apparently is an instance of congenital heart block." Dr. Cary Eggleston, who saw the patient in the ward, commented in part: "The electrocardiogram establishes definitely the existence of a complete structural block in the bundle of His, with resulting auriculoventricular dissociation. Since the ventricular complexes, which are a result of transmission of impulse through the Purkinje system, are normal in contour, the impulse which gives rise to them must be developed high up in the course of the main bundle. It follows that the lesion responsible for the block must be above this level. This places the lesion, which is probably a ventricular septal defect, close to the auriculoventricular septum. Pneumonia, measles and

other acute infectious diseases to which infants of this age are subject are practically never responsible for permanent structural damage to the bundle. It seems improbable, therefore, that infection has any causal relationship in this case."

The subnormal temperature present on admission was readily overcome. During the first two weeks in the hospital there were occasional sessions of mild fever up to 101 F., which were associated with scattered and transient râles in the lungs. During the last week of the patient's stay in the hospital, she was free from these symptoms. She was fed evaporated milk, water and added carbohydrates, with a caloric intake of from 105 to 150 calories per kilogram. She gained fairly well for the first week, then gradually lost weight and was discharged, on June 27, 1926, unimproved. She weighed practically the same when discharged as when she was admitted. She died at home, July 4, 1926. Autopsy was not performed.

135 East Fifty-Fifth Street.

SCARLET FEVER

I. THE RELATION BETWEEN ANTITOXIN IN THE BLOOD AND SKIN SENSITIVITY TO TOXIN IN NEW-BORN INFANTS AND IN THEIR MOTHERS *

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WITH THE TECHNICAL ASSISTANCE OF
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Since the demonstration [1] (Dicks) in filtrates of scarlatinal streptococci of a toxin which causes a skin reaction in certain persons apparently susceptible to scarlet fever and none in others apparently immune, there has been a tendency to draw a close analogy between the interpretation of Dick tests in relation to scarlet fever and that of the Schick test in connection with diphtheria. It has been assumed that a negative Dick test shows a true antitoxic immunity to scarlet fever; this has been supported by the presence of an antitoxin in serums from patients convalescing from scarlatina and from others in whom the Dick tests were negative which, when added to toxin, neutralizes its toxic action in the skin of a susceptible person. The nature of the skin reaction, its relation to immunity, antitoxin and streptoccocic infection, and the identity of their apparent analogies to the known pathologic processes in diphtheria are of fundamental importance, and an attempt has been made to study these phenomena experimentally.

The present paper deals with observations made on 200 mothers and their infants in the first ten days of life and again from six weeks to three months later. The reaction of the skin to varying amounts of toxin, the presence of demonstrable amounts of antitoxin in the blood and the relation of antitoxin to the skin reactions were studied. There is no record of similar previous studies.

In this connection it is of some interest, for the purpose of comparison, to quote briefly the results of a series of observations by von

* Received for publication, July 20, 1927.

* From the Department of Pediatrics of Washington University School of Medicine, the Barnes Hospital, and the Shriner's Hospital for Crippled Children, St. Louis.

1. Dick, G. F., and Dick, G. H.: A Skin Test for Susceptibility to Scarlet Fever, J. A. M. A. **82**:265 (Jan. 26) 1924.

Gröer and Kassowitz [2] on very young infants in whom they compared the immunity to diphtheria as indicated by the Schick test with that shown by the demonstration of antitoxin (Römer's method). Although the toxin used by them gave pseudoreactions in a number of older children and adults, the rarity of such reactions in the very young allows the acceptance of their figures in the instances to be quoted. In 143 new-born infants, 16 per cent did not show any antitoxin in the blood and in 5 per cent the Schick test was positive; while in 57 infants, from 3 weeks up to 3 months of age, 29 per cent did not have antitoxin, and 28 per cent had Schick tests that were positive. There was a similar correspondence of 44 and 43 per cent in other infants from 3 to 6 months old. It would seem from the foregoing that while the skin of new-born infants whose blood does not contain antitoxin reacts to diphtheria toxin in only about one third of the cases, before 3 months of age the skin has acquired this reactive ability in all instances.

MATERIAL AND METHODS

The infants and mothers were from the white obstetric wards of the Barnes Hospital, and the tests were made by permission of Dr. Otto Schwarz. The obstetric patients were admitted consecutively to the ward during eight months and were unselected. Skin tests were made on both with 2, 20 and 50 standard skin test doses (STD) of a scarlatinal streptococcic filtrate containing 100,000 STD per cubic centimeter when the infants were from 2 to 8 days old. Blood for antitoxin tests was obtained a day or two later. Retests were made on infants between the ages of 6 weeks and 3 months. All tests were read in twenty-four hours. It is somewhat more difficult to make intradermal injections into the new-born than it is to make such injections later on account of a toughness of the dermis which offers considerable resistance to the injection.

The scarlatinal toxin used did not give any pseudoreactions in a number of trials with heated preparations, so that routine heated control tests were not carried out.[3] The amounts of original filtrate injected were 0.00002 cc. (2 STD), 0.0002 cc. (20 STD) and 0.0005 cc. (50 STD) in dilutions so that the dose was always 0.1 cc.

The reactions were read positive when they reached 1 cm. or more in any diameter, irrespective of whether the erythema was bright red or the faint "ghost" reaction. Some areas of reaction smaller than 1 cm. in diameter were

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2. Von Gröer, F., and Kassowitz, K.: Studien über die normale diphtherieimmunität des Menchen: II. Ueber das Verhalten des normalen Diphtherieantitoxines bei Mutter und Neugebornem, Ztschr. f. Immunitätsforsch. u. exper. Therap. **23**:108, 1915; IV. Die Normale Diphtherieimmunität im Kindersalter, ibid. **28**:327, 1919.

3. The toxin used was furnished through the kindness of Mr. F. G. Jones of the Eli Lilly Biological Research Laboratories. In its preparation no blood was employed, and the strain of streptococcus used was originally obtained from Dr. W. H. Park and labeled "Park 1803." This preparation was particularly suitable on account of its high potency and freedom from pseudoreactions in the dilutions used. In a large number of tests in cases of scarlet fever and on normal children the results have apparently been constant and reliable.

considered partial reactions but were included in the negatives, on account of the difficulty of distinguishing them constantly from the small areas which sometimes result from the trauma caused by the needle. As would be expected, if the test with 2 STD was positive, larger doses gave larger reactions, the areas sometimes reaching 3 or 4 cm. In the infants the areas of positive reactions were, as a rule, somewhat smaller than in older persons and usually somewhat indurated.

Blood was tested for antitoxin in the following manner: To 0.6 cc. of sterile serum was added 12 STD of toxin diluted to 0.3 cc. This mixture was incubated at least an hour, and 0.15 cc. (0.1 cc. serum with 2 STD of toxin) was injected intradermally into children with known positive Dick reactions to 2 STD or less. A negative test shows the presence of sufficient antitoxin to neutralize 20 STD per cubic centimeter in the serum, whereas a positive reaction indicates less than that amount. A small amount of antitoxin would not be recognized by this test, but the opportunities for error appear greatly increased by attempting to determine in a routine manner smaller quantities in a large series. In general, antitoxin can be recognized in this way in serum from persons whose skin does not react to 20 STD, although when the skin is sensitive to smaller quantities of toxin, the presence of antitoxin is not always demonstrable.

The skin tests for neutralization of toxin were done by permission of Dr. Leroy Abbott, at the Shriners' Hospital for Crippled Children, on healthy patients who were undergoing corrective orthopedic treatment. Each serum was tested on four children who had positive reactions to the Dick test in order to eliminate possible technical errors. Preliminary control skin tests with mixtures of toxin and serum from a person showing a positive reaction to the Dick test had been made on all children used for neutralization tests. In some children with positive reactions to the toxin alone, the toxin was apparently neutralized in such a mixture, although tests on other children did not show neutralization. No adequate explanation of this phenomenon is offered, but it necessitated the use of only those children who were found suitable by preliminary tests. Almost all of the results were identical, but occasionally one test would show a variation. Sometimes this was shown to be due to the fact that a child's reaction to the Dick test had become negative as a result of previous successive intradermal injections of test toxin, while in other instances no explanation was apparent. Such inconsistencies were observed so infrequently that no exception to the general results could be based on them.

The recorded tests for antitoxin are based on the readings made after twenty-four hours. Some tests, in which toxin was apparently completely neutralized for twenty-four hours, appeared positive after forty-eight hours. Although it seems probable that a complete inhibition indicates a higher antitoxin content than that which persists only twenty-four hours, no attempt was made to titrate any serums for quantity of antitoxin; the recorded tests, therefore, show only the presence or absence of small demonstrable amounts of antitoxin. The close supervision, both clinical and serologic, of all patients used in this study has reduced the danger of any cross syphilitic infection to a minimum. No infection of any kind has resulted from skin tests.

In a few tests in which mother's or infant's serums were examined for antitoxin by neutralization tests, the serums were also tested for their power to blanch early scarlatinal eruptions locally. In 0.5 cc. amounts the blanching tests agreed with the neutralization tests in every instance tried. The same correspondence in both qualitative tests for antitoxin has been observed in serums from other sources.

The results will not be detailed individually but have been tabulated (tables 1 to 4). The constant use of varying amounts of toxin in the skin tests allows a grouping of the individuals into four classes, which, for the sake of simplifying reference to them, will be called (1) very sensitive, or those whose skin reactions are positive to small amounts of toxin (2 STD); (2) moderately sensitive, those whose skin reactions are positive to 20 STD but negative to 2 STD; (3) slightly sensitive, those whose reactions are positive to 50 STD but negative to 20 STD; and (4) negative, those whose reactions are negative to 50 STD.

SKIN REACTIONS OF MOTHERS AND NEW-BORN INFANTS

In table 1, 200 mothers have been grouped in the classes mentioned in the foregoing paragraph in accordance with their reactions to the skin tests, and the reactions of the infants of the mothers in each group have been similarly arranged. In three twin pregnancies of the series,

TABLE 1.—*Degree of Skin Sensitivity to Scarlatinal Toxin in New-Born Infants and Their Mothers*

Mothers' Skin Reactions	Number	Infants' Skin Reactions			
		—	+50 STD	+20 STD	+2 STD
Positive 2 STD	53	32	10	9	2
Positive 20 STD	54	47	6	1	0
Positive 50 STD	42	42	0	0	0
Negative	51	51	0	0	0

both infants' reactions were identical, and each pair was considered as a unit in the tabulation.

A definite history of previous scarlet fever was obtained in only a few mothers, since most of them did not know whether they had had the disease or not. Of the thirteen who were certain of having had it, all were negative to 2 STD except two. It will be noted that fifty-three of the two hundred or 26.5 per cent of all mothers were very sensitive, a proportion of positive Dick tests comparable to that described in adults. The others did not react to small amounts of toxin, but fifty-four were moderately sensitive and forty-two were slightly sensitive, while fifty-one gave negative reactions.

In the entire group of 200 infants, 172 (86 per cent) were negative even to the largest amount of toxin used (50 STD) and only two (1 per cent) were positive to 2 STD. When these infants' reactions are considered with reference to their mothers' tests, however, it is seen: (1) that all the infants giving positive reactions in any degree had mothers whose skins were very sensitive or moderately sensitive; (2) that more than three fourths of these infants with positive tests

had mothers who were very sensitive, and (3) that when the mothers' tests were negative or only slightly sensitive, the infants' tests were always negative.

In this connection it might be mentioned that Zingher [4] found antitoxin in four of six specimens of blood from the umbilical cord, and in each instance in which antitoxin was present, the mother and infant gave a negative Dick reaction, while in the two cases in which no antitoxin could be detected, both mother and infant gave positive Dick reactions. This close correlation between the infants' and mothers' skin tests and the presence of antitoxin in their blood is quite at variance with our observations, which revealed only two infants with positive Dick tests out of fifty-three whose mothers' tests were positive.

The fact that the Dick test is negative in the new-born has been mentioned by several observers, Kunz and Nobel,[5] for example, having found only one positive Dick test in seventy-four infants, but it is of interest that such a large number of infants also failed to react to rather large skin doses of toxin. This was somewhat more unexpected in those infants whose mothers were very sensitive to toxin, 60 per cent in this group giving negative tests to 50 STD and only 4 per cent being as sensitive as their mothers. In the babies whose mothers were less sensitive, the lack of skin sensitivity could presumably be attributed to antitoxin transmitted from the mother to the infant. Even with such an assumption, it seems unusual that most of these infants, as judged by the skin tests, should apparently have a greater immunity than their mothers. The relation of antitoxin to skin sensitivity has been studied further.

THE RELATION OF ANTITOXIN TO SKIN SENSITIVITY TO TOXIN

It is generally stated that a positive Dick test indicates the absence of antitoxin, and a negative Dick test shows an antitoxic immunity. Although relatively few observations on this point seem to have been made, the few that have been reported indicate that there may be exceptions. The actual proportion of such exceptions is not known, and may be small. Henry and Lewis [6] found no antitoxin in two adults and in two children, all of whom were skin sensitive to small amounts of toxin, and demonstrated antitoxin in three adults and in one child whose skins were negative to small doses but reacted to larger amounts.

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4. Zinger, A.: The Dick Test in Normal Persons and in Acute and Convalescent Cases of Scarlet Fever, J. A. M. A. **83**:432 (Aug. 9) 1924.

5. Kunz, H., and Nobel, E.: Die Dicksche Hautreaktion als Prüfung der Scharlachimmunität: IV. Mitteilung Untersuchungen an Schwangeren und Wöchnerinnen, Ztschr. f. Kinderh. **42**:372 (Nov. 6) 1926.

6. Henry, H., and Lewis, F. C.: Immunity to Toxin of Streptococcus Scarlatinae, Lancet **209**:587 (Sept. 19) 1925.

Davies,[7] in testing seventeen persons five months or more after an attack of scarlet fever, found that although antitoxin could be demonstrated in all except one, seven showed some skin reaction to 1 STD. Other mention of isolated quantitative tests for antitoxin, usually in persons having negative reactions to the Dick test, is found in the literature on the subject, and occasional instances of the presence of antitoxin in a person with a positive reaction to the Dick test have been noted.

Some of the mothers have been examined for antitoxin, and, as will be seen from table 2, no antitoxin was demonstrable in those whose skins reacted positively to a small amount of toxin, while in those giving negative skin tests to 2 STD antitoxin was almost always found. The series tabulated is small, but the general correspondence in these results and those in a number of other tests carried out on adults and on older children is such that further determinations on mothers was

TABLE 2.—*Relation of Presence of Antitoxin in Mothers' Blood to Their Skin Sensitivity to Toxin and to Infants' Antitoxin*

		Antitoxin			
		Mothers		Infants	
Mothers' Skin Reactions	Number	+	—	+	—
Positive 2 STD	5	0	5	0	5
Positive 20 STD	5	4	1	2	3
Positive 50 STD	4	4	0	3	1
Negative	6	6	0	4	2

thought unnecessary. The single exception in which no antitoxin was found, although the skin test was negative to 2 STD but positive to 20 STD, may be an example of the inability of the method used to detect regularly small amounts of antitoxin. For example, in tests on other persons whose reactions were negative to 2 STD but positive to 5 STD, we have been unable to detect antitoxin; but if the skin test was negative to 10 STD, antitoxin has almost always been demonstrable. It seems likely that this mother, although the test with 2 STD was negative, was skin sensitive to a slightly larger amount, and that her blood contained too small a quantity of antitoxin to be recognized by the method used.

Another point of interest in table 2 is the relation between antitoxin in the blood of a mother and in the blood of her infant. Whenever antitoxin was found in the infant's blood, it was always demonstrable in the mother's; but in certain instances when antitoxin was readily

7. Davies, J. A. V.: Studies in Scarlet Fever: IV. Post-scarlatinal Immunity in Patients Treated with Antitoxin, J. Clin. Investigation **3**:423 (Dec. 20) 1926.

demonstrable in the mother's blood, none was found in the baby's blood. While this does not exclude the presence of antitoxin in the infants of immune mothers, it is apparent that any antitoxin present is small in amount and distinctly smaller in quantity than in the maternal blood. This corresponds with experimental observations on the transmission of immune substances, that the immune bodies in the offspring are less in amount than in the mother.

The assumption that antitoxin is present in the majority of mothers in whom the skin is negative to small doses of toxin even though it may react to larger amounts, is apparently justified from the results shown in the previous table (table 2).

In table 3 the results of antitoxin determinations in fifty-four infants are tabulated with relation to their own and their mother's skin sensitivity to toxin. This, it will be seen, is a somewhat more extended study of the presence of antitoxin in the new-born than that

TABLE 3.—*Relation of Antitoxin in Blood of New-Born Infants to Their Mothers' Skin Sensitivity to Toxin*

Mothers' Skin Reactions	Number Tested	Infants' Skin Reactions							
		— Antitoxin		+50 STD Antitoxin		+20 STD Antitoxin		+2 STD Antitoxin	
		+	—	+	—	+	—	+	—
Positive 2 STD.	20	0	13	0	4	0	2	0	1
Positive 20 STD.	10	6	1	1	1	0	1	..	..
Positive 50 STD.	9	7	2	..	..	..	..	..	..
Negative.	15	13	2	..	..	..	..	..	..

shown in table 2, and includes the infants from that table. The results confirm those of the previous table in that antitoxin was never found in infants whose mothers' skin test were positive to 2 STD. This absence of antitoxin had no relation to the presence or absence of a positive reaction to toxin in the infant's skin, since many infants without antitoxin gave negative skin reactions to considerable amounts (50 STD) of toxin. Antitoxin was usually demonstrable in the other infants, whose mothers were presumably immune since they were not skin sensitive to a small dose of toxin, although they reacted to larger amounts. In some of these babies, as noted previously in table 2, the amount of antitoxin, if present, was too small to be detected.

COMPARISON OF INFANTS' SKIN REACTIONS AT BIRTH AND LATER

In table 4 are found the skin reactions at from six weeks to three months after birth of eighty of the infants who had been tested when only a few days old. The first skin reactions of the infants, as well as those of their mothers, are also shown for comparison. In the later tests on the group of infants whose mothers were very sensitive, a con-

siderably increased proportion showed some skin sensitivity to toxin, although only about one-third became sensitive to 2 STD. The later tests on the infants whose mothers were positive to 20 STD also showed that a number had become somewhat more sensitive, although the tests of many were still negative to a considerable amount of toxin. Those babies whose mothers were least sensitive and who required 50 STD or more to give a positive skin reaction, exhibited the least change in later skin tests. It is evident that the appearance of skin sensitivity in infants within three months after birth has a direct relation to the degree of skin sensitivity of the mother, and that the tendency to develop this sensitivity is most marked in babies whose mothers are very sensitive. The presence of antitoxin in the infant as a result of placental transmission from the mother is not the only factor in the delay in appearance of skin sensitivity, since infants of nonimmune

TABLE 4.—*Comparison of Skin Sensitivity of Infants at Birth and Later*

Mothers' Skin Reactions	Number Retested	Infants' Skin Reactions						
		At Birth			6 Weeks to 3 Months			
		—	+50 STD	+20 STD	—	+50 STD	+20 STD	+2 STD
Positive 2 STD.....	17	11 ..	2	.. 4	3 1	2 ..	4 .. 4	2 1
Positive 20 STD.....	21	18	.. 3	.. ..	11 1	4 1	3 1	
Positive 50 STD.....	22	22	..	..	20	1	..	1
Negative.....	20	20	..	..	18	2		

mothers are sensitive to small amounts in only a few instances, and some are insensitive to rather large amounts of toxin. In general, in the entire group of infants, at birth 14 per cent showed some sensitivity to toxin and 1 per cent were very sensitive, while the retests later showed 33 per cent with some sensitivity and 5 per cent very sensitive.

Retests were also made on thirty-three of the mothers to determine whether their degree of skin sensitivity remained the same after from one and one-half to three months. In twenty-four the second tests were quantitatively identical with the first, while in nine there were slight differences. These included three whose first tests showed that they were slightly sensitive and whose later tests were negative; three who had been moderately sensitive and were slightly sensitive later; one very sensitive who was later moderately sensitive, and two who had been slightly sensitive became moderately sensitive later. The only significance of such changes seems to be that they indicate that slight alterations in the degree of skin sensitivity of adults may occur when tests are done at different times.

COMMENT

The lack of skin sensitivity to scarlatinal toxin in the new-born and its apparently irregular and incomplete appearance in early infancy offer an explanation of the rarity of clinical scarlet fever at this time of life. The reasons for the absence of skin reactivity, however, are not apparent. At first thought, the presence of antitoxin derived from an immune mother through the placenta seems a possible source of the failure of the infant's skin to react, but a large number of infants of nonimmune mothers are insensitive also. This seems to correlate with the observed clinical phenomena that young infants remain free from the disease even though born or suckled by mothers with active scarlet fever. It is true that after two or three months the infants of immune mothers show less sensitivity than those of nonimmune mothers. It is not logical to assume a greater concentration of antitoxin in the blood of an infant than in the blood of its mother, and there is some evidence that the infant's blood contains less, so that if the presence of antitoxin from the mother were the only cause for the inhibition of the infant's skin reaction, the sensitivity of the infant should be at least as great as that of the mother. This was true in only one fifth of the babies up to 3 months of age. It seems apparent that the development of skin sensitivity to scarlatinal toxin in early infancy is inconstant and gradual, and that, while the presence of antitoxin may delay the appearance of skin sensitivity, the absence of reactivity in the skin is due to other factors.

Since other observations of skin sensitivity to intradermal injections of toxin in the new-born and early infancy have been made with diphtheria toxin, a comparison of the Schick test at this age and the Dick test is of some interest. Mention has been made of the early observations of von Gröer and Kassowitz,[2] who found positive Schick tests in only 5 per cent of the new-born and no antitoxin in the cord blood of 11 per cent of the remainder. Such a low incidence of positive reactions to the Schick test in the new-born has not always been observed in the studies of others. Ruh and McClelland,[8] in Cleveland, for example, found positive reactions in 21 per cent of 100 infants, while Kittner and Ratner[9] in New York reported 8 per cent positive reactions in 50 babies. All these observers noted a certain small number of infants with negative reactions whose mothers gave positive reactions to the Schick test, but in none was the discrepancy comparable

8. Ruh, H. C., and McClelland, J. E.: Comparison of the Diphtheria Immunity in the Mother and in the New-Born, Am. J. Dis. Child. **25**:59 (Jan.) 1923.

9. Kuttner, A., and Ratner, B.: The Importance of Colostrum to the New-Born Infant, Am. J. Dis. Child. **25**:413 (June) 1923.

with the figures reported here of only 4 per cent of positive Dick tests in infants whose mothers' tests were positive. The same discrepancy between the skin sensitivity to diphtheria toxin and to scarlatinal toxin as evidenced by Schick and Dick tests is still present in the first two or three months of life. These marked differences and the fact that a negative Schick test is rather closely dependent on the presence of diphtheria antitoxin, while a negative Dick test is not so closely associated, suggest that there may be fundamental differences in the development of skin sensitivity in the two conditions.

SUMMARY

The skin of new-born infants rarely reacted to a small amount (2 STD) of scarlatinal toxin, and reacted to larger amounts in only a small proportion of cases. This skin sensitivity, when present, occurred only in infants of mothers who were sensitive to 20 STD of toxin or less.

In mothers whose skin was sensitive to small amounts of toxin, no antitoxin was found in the blood. In their infants, lack of skin sensitivity to toxin was not dependent on the presence of antitoxin in the blood, since many without antitoxin were insensitive. In mothers who gave negative skin reactions to small amounts, antitoxin was almost always demonstrable, while in infants of such mothers antitoxin was not always found.

When a number of the same infants whose skin sensitivity had been tested at birth were retested between the ages of from 6 weeks and 3 months, there was some skin reactivity to toxin in about one-third, but only a few were sensitive to small amounts. This development of sensitivity to toxin occurred in a larger proportion of infants of very sensitive mothers than in those whose mothers were less sensitive to toxin.

CONCLUSIONS

In the new-born, the skin is usually not sensitive to considerable doses of scarlatinal toxin, although occasionally some sensitivity is present. This lack of skin sensitivity is not due to the presence of antitoxin. After some weeks, the skin may develop sensitivity, which is evidenced first by positive reactions to larger amounts of toxin. During the first months of life, skin sensitivity appears in a larger proportion of infants who had no antitoxin in the blood at birth than in those whose blood contained antitoxin.

FEVER IN THE NEW-BORN *

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The material for this paper has been secured from the hospital records of the new-born in three maternity nurseries, one covering a period of two years and the other two a period of one year each.

The temperature of the babies was taken twice daily, at 9 a. m. and at 4 p. m., by rectum, the thermometer being inserted 1½ inches (3.81 cm.) for a two minute period. If fever developed, the temperature was taken every three hours until a normal temperature was reached and maintained.

The rectal temperature of a new-born baby varies 3 or 4 degrees during the first four or five hours following birth, as shown in table 1. This is dependent, first, on the type of delivery, and second, on the length of time during which the infant is exposed. The initial bath of water at a temperature of 100 degrees nearly always causes a fall in the baby's temperature. After a period of about six hours, the temperature returns to what is considered as normal, varying between 97 and 99 degrees. In this group of cases, a baby is considered to have had fever when the temperature by rectum is 100 F. or more.

INCIDENCE

In studying the incidence, the following observations were made, as shown in table 2. Of 1,246 babies cared for in the Philadelphia Lying-In Hospital, 94 or 7.5 per cent developed fever; of 428 new-born babies in the maternity ward of the Jefferson Medical College Hospital, 67 or 15.6 per cent had fever; of 298 babies in one of the private nurseries of the Jefferson Medical College Hospital, 63 or 21.1 per cent had fever. These figures comprise a total of 1,972 babies, with fever in 224, or 14.7 per cent. In a study of 817 babies, Adair and Stewart [1] found that 12.2 per cent developed fever during the first week of life.

ETIOLOGY

Among the causes of fever in the new-born were various pathologic conditions, as shown in table 3. In this series there were 3 cases of pyelitis, 3 of pneumonia, 1 of otitis media, 2 of burns caused by a hot

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* From the Departments of Obstetrics and Pediatrics, Jefferson Medical College.

1. Adair, F. L., and Stewart, C. A.: Fever in New-Born Infant, Am. J. Dis. Child. **31**:846 (June) 1926.

water bottle, 2 of erysipelas, 2 of diarrhea and 211 cases of dehydration. The term "inanition" is also given to the latter group of cases.

There are several possible sources of error in the dehydration group. Other pathologic conditions, not detected may have been present as the real cause of the fever; also, certain babies delivered by considerable

TABLE 1.—*Variations in Rectal Temperatures of New-Born Infants*

	Normal Delivery		Version Delivery	
	Rectal	Temperatures	Ether	Anaesthesia
	P. M.		P. M.	
Born	9:50	99.8	Born 9:10	96.8
	10:00	97.6	9:20	96.0
	10:10	97.2	9:30	95.6
	10:20	97.6	9:40	95.4
	10:30	98.0	9:50	95.6
	10:40	98.2	10:00	95.6
	10:50	98.6	10:10	95.0
Bath	11:10	98.6	10:30	95.6
	11:30	98.8	10:50	95.4
	11:50	98.6	Bath 11:10	95.6
	A. M.	....	11:30	95.6
	12:10	98.0	11:50	96.0
	12:30	97.8	A. M.	....
	12:50	97.8	12:10	96.0
	1:10	97.8	12:30	96.4
	1:30	98.0	12:50	96.6
	1:50	97.8	1:10	96.6
	2:10	98.0	1:30	97.2

TABLE 2.—*Incidence of Cases of Fever*

Nursery	Total Cases	Fever Cases	Per Cent
Philadelphia Lyin-In	1,246	94	7.5
Jefferson—ward	428	67	15.6
Jefferson—private	298	63	21.1
Totals	1,972	224	14.7

TABLE 3.—*Pathologic Conditions as Causes of Fever in New-Born Infants*

Pyelitis	3
Pneumonia	3
Otitis media	1
Burns	2
Erysipelas	2
Diarrhea	2
Dehydration	211

manual stress may develop a fever spoken of as "aseptic." It is believed that the trauma of the delivery is sufficient to cause a certain amount of subcutaneous and intramuscular exudation which, on absorption, gives rise to fever. Some observers believe that these are cases of cerebral hemorrhage.

Conrad [2] emphasizes the importance of pyelitis in the new-born. He speaks of it as "congenitally acquired pyelitis." Information concern-

2. Conrad, C. E.: Congenitally Acquired Pyelitis, Am. J. Dis. Child. **31**:253 (Feb.) 1926.

ing the entrance of bacteria into the blood stream of the new-born is increasing, and more cases are being found showing a real bacteremia.

Chart 1 shows a typical temperature curve and weight curve for a case of dehydration, a case of pyelitis and one of burns caused by a hot water bottle. A sudden rise of temperature and then an equally sudden fall after appropriate treatment is a characteristic of dehydration fever, so that the elevation of temperature may last for a period of only from six to twelve hours. The sudden drop to normal temperature may take place in from one to two hours. In the typical case of dehydration fever, the temperature then maintains a normal course; in other cases, such as pyelitis, burns and pneumonia, the temperature will fluctuate for two or more days.

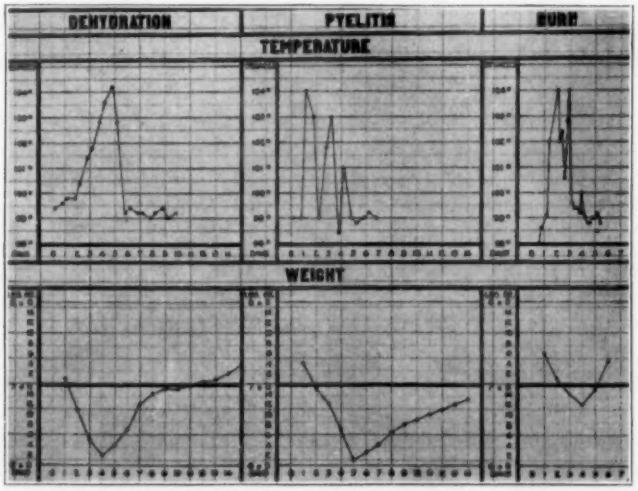

Chart 1.—Typical temperature curve and weight curve in a case of dehydration, a case of pyelitis and one of burns.

Other etiologic factors that must be considered are shown in table 4. The loss of weight in 200 normal cases was 7.7 per cent of the weight at birth; in the 224 cases of fever, 10.3 per cent, or 2.6 per cent more than in the normal cases. The day of the lowest weight in ninety-four fever cases was 4.2 days after birth; in ninety-four normal cases, 4.6 days after birth.

A number of authorities speak about the greater incidence of fever in the baby of the primiparous mother. Observations were made in 151 cases, with 53 per cent multiparous patients and 47 per cent primiparous patients. Of the 224 infants with fever, 91 per cent were full term and 9 per cent premature babies.

The type of delivery was observed in 200 cases. Half of the babies were delivered by operation, that is, by cesarean section, version or forceps, during which an anesthetic was given. Twelve of the babies developed fever. The other 100 were delivered normally, and eight developed fever. The day the fever occurred was observed in 130 cases, and the average was found to 4.3 days after birth. This corresponds with the day of low weight, which in cases of fever was 4.2 days.

In chart 2 is shown the weight curve in a normal case in which the infant did not have fever. The loss in this case is equivalent to 9 per cent of the weight at birth. The baby lost weight for two days and then gained, reaching the weight at birth on the ninth day.

In chart 3 is shown a weight chart of a baby who lost 27 per cent of its natal weight and yet did not develop a fever. This case is interesting also, because on the seventeenth day there was a sudden loss in weight and the infant died. The cause of the death was not determined

TABLE 4.—*Other Etiologic Factors Found in New-Born Infants*

Weight loss	Normal [200]	7.7%	Fever cases (224)	10.3%
Day of low weight.....	Normal (94)	4.6	Fever cases (94)	4.2
Para (151)	Multipara	53%	Primipara	47%
Term (224)	Full term	91%	Premature	9%
Delivery (200)	Anesthesia operation	12%	Normal	8%
Day of fever.....	130	4.3 da.		

clinically, but autopsy showed an acute hemolytic streptococcic peritonitis. The mother of the baby had an acute tonsillitis from which the same organism had been recovered. Apparently the baby ingested the organism with its food.

SEASONAL OCCURRENCE

In the series of cases reported by Adair and Stewart,[1] they found that 87.8 per cent of their cases occurred from May to September, and, while they report the total incidence of fever in the new-born to be 12.2 per cent, the incidence of fever in the babies born during the five months mentioned was 24.3 per cent.

It is noted in chart 4 that in this series of 224 cases only 31 per cent occurred in the so-called hot months of May, June, July, August and September. The incidence of fever in the 820 babies born during the five summer months was 9 per cent, but varied for the three nurseries 7 per cent, 15 per cent and 6 per cent, respectively. During the period of two years there was only one month, namely, June, 1925, in which a number of the cases of fever were probably due to the excessive external temperatures.

In chart 5, the occurrence of fever, according to months is graphically described for the three nurseries concerned. It shows that the incidence of fever varies for the different nurseries during the same time. In March, 1926, there were sixteen cases of fever in one nursery, three in another and none in another. Apparently the seasonal occurrence of fever in the new-born has had little influence in the series reported.

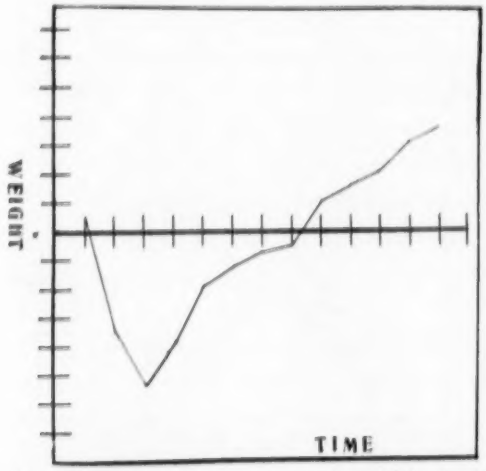

Chart 2.—Weight curve in a normal case in which the infant did not have fever.

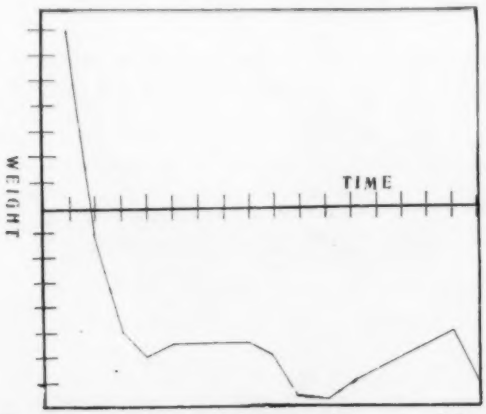

Chart 3.—Chart showing loss in weight of a baby who did not develop fever.

However, several of the cases of dehydration fever in premature babies were evidently due to the fact that the infants were overheated in the incubators. The greater incidence of fever among the private patients can possibly be accounted for by the excess of clothing. These factors amount to practically the same thing as excessive external temperature.

BACTERIAL INVASION

The question of bacterial invasion or the absorption of toxic products from bacteria as a cause of fever in the new-born has been brought forward at intervals, but has never been definitely proved. It has been recognized for some time that the gastro-intestinal tract of new-born infants is rapidly invaded by various organisms. Attention was drawn to this fact by the prompt response secured by colonic irrigation in

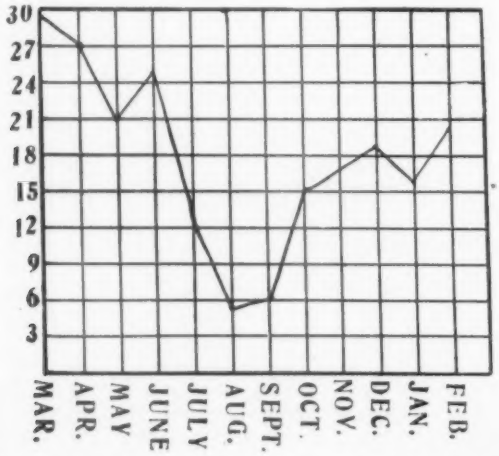

Chart 4.—Seasonal occurrence of fever in the new-born infant.

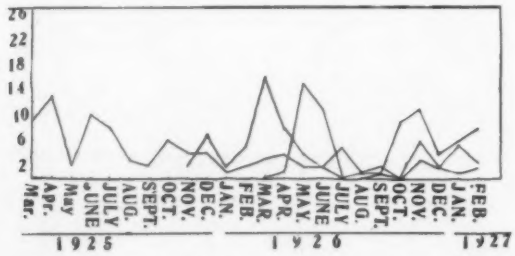

Chart 5.—Seasonal occurrence of fever in the new-born infant as recorded in three different nurseries.

some cases of fever. In many cases reported in this paper, colonic irrigation was given as soon as fever was noted. The effects of the irrigation were as prompt, and in some cases more prompt, than when extra fluid was given by mouth. This suggested the possibility of bacterial colonization in the rectum.

In table 5, a result of rectal cultures is shown. These cultures were all taken during the first twenty-four hours following birth. A total of 33 cases was studied; 2 were sterile, 18 showed *Bacillus coli,*

17 showed *Staphylococcus,* 10, *Streptococcus hemolyticus,* 2, *Streptococcus viridans,* 7, *B. proteus* and 2, *B. subtilis.* Several babies had positive cultures within the first four hours. These cases were studied without reference to the question of fever. Three of the babies in this group later developed fever.

It has been known for some time that breast-fed babies have more resistance to disease than bottle-fed babies, and also that the blood serum of breast-fed babies has more bactericidal properties than the blood serum of bottle-fed babies. Immunity may be obtained through placental transference or by means of the breast secretion, colostrum and breast milk, or the infants may develop immunity.

Lewis and Wells [3] discuss the function of the colostrum exhaustively. I quote their summary in full.

The blood of new-born infants, and probably of all other mammals, contains little or none of the serum protein or protein fraction known as the euglobulin. This seems to be supplied chiefly by the colostrum, which differs from milk in containing a large amount of this protein secreted directly from the blood. The euglobulin is the only blood protein that appears in the colostrum, and it is the only protein fraction in which the new-born infant's blood is deficient. Evidently the colostrum is formed to provide the fetus with a supply of euglobulin for its blood during the short period immediately after birth when proteins may be best absorbed without disintegration by digestive proteolysis. The importance of this lies in the fact that the protective antibodies of the blood are found associated with the euglobulin fraction, and that the quantity of protective antibodies found in the colostrum the milk and the infant's blood varies directly with the euglobulin content of these fluids. Evidently the colostrum furnishes to the new-born mammal protective antibodies, which probably add much to its capacity to resist infection in early life. If the infant does not receive colostrum it acquires euglobulin in its blood much more slowly, and presumably is in corresponding degree less resistant to infection. It is not probable that there is any equivalent substitute for human colostrum for new-born infants.

TABLE 5.—*Results of Rectal Cultures Taken Twenty-Four Hours Postnatal*

Total cases	33
Sterile	2
B. coli	18
Staphylococcus	17
Streptococcus hemolyticus	10
Streptococcus viridans	2
B.proteus	7
B. subtilis	2

Theobald Smith and his co-workers at the Rockefeller Institute, department of animal pathology, have discovered that the colostrum of the cow is the chief agent for transferring antibodies to the new-born

3. Lewis, J. H., and Wells, H. G.: Function of Colostrum, J. A. M. A. **78**:863 (March 25) 1922.

calf. Calves which have never received colostrum are extremely likely to succumb during the first week of life by common infection of the alimentary tract with organisms of the *B. coli* group.

However, Kuttner and Ratner [4] reported that the human placenta was permeable to diphtheria antitoxin, and that they were able to find diphtheria antitoxin in appreciable amounts in the cord blood of newborn babies. Methylene blue given to mothers for a few days prior to delivery passes readily into the baby. The baby will void the dye during the first day after birth.

There is a distinct relation between the loss of weight in babies, the inability of the child to get breast secretion in the first few days, the occurrence of fever and the question of bacterial invasion.

PREVENTION

If dehydration fever is due solely to the lack of water, fever should be prevented by giving an abundance of water. In March, 1925, forty-five babies were given a daily average of 4 ounces (118 cc.) of

TABLE 6.—*Results of Giving Water and Food to Prevent Fever*

1925	Number Cases	Water or Food	Daily Average	Number Fever Cases
March	45	Water	4 oz.	9
April	50	5% Glucose	2 oz.	13
May	46	5% Glucose	1 oz.	2
July	60	Whole milk ⅓ sugar 2.5%	4 oz.	8
August	57	Whole milk ⅓ sugar 2.5%	4 oz.	3
September	49	Whole milk ⅓ sugar 2.5%	4 oz.	2

boiled water in addition to breast feedings; nine cases of fever occurred. In April, fifty babies were given a daily average of 2 ounces (59 cc.) of 5 per cent dextrose; thirteen cases of fever developed. In July, sixty, in August, fifty-seven and in September, forty-nine babies were given 4 ounces of one-third whole milk daily, two-thirds boiled water and 2.5 per cent sugar. Fever developed in eight, three, and two babies, respectively, during those months. The data are shown in table 6.

In the prevention of dehydration fever, another factor is of greater importance than the giving of extra water or artificial food. Proper supervision of breast feeding in the first few days of life to make sure that the baby gets its full quota of colostrum and breast milk will do more to prevent dehydration fever than any other possible factor.

From March, 1925, to March, 1926, of 568 babies in one of the nurseries, 64 or 11 per cent, developed fever. It was during this time that additional food and water were given to each baby. From March, 1926, to March, 1927, of 678 babies 30, or only 4.4 per cent, developed

4. Kuttner, A. G., and Ratner, B.: Importance of Colostrum to New Born Infant, Am. J. Dis. Child. **25**:413 (June) 1923.

fever. It was during the latter period that full supervision was given to the nursing of the babies in the first few days.

In the private nursery spoken of, it is a custom for each patient to have her own special nurse, in many instances two special nurses, one for day and one for night duty. Consequently, in a private nursery of twenty beds there may be from twelve to twenty different nurses taking care of the babies. When two nurses are on duty, each sleeps in her own room, returning to the maternity department every day. It is obvious that the greater number of persons in the nursery, the greater the possibility of infection as well as of faults in nursery technic.

PROGNOSIS

The prognosis in the cases of fever is shown in table 7. The gain in weight of 200 normal babies was 9.4 ounces (262.23 Gm.) in the period of two weeks, during which they stayed in the nursery. Of the 224 cases of fever, the gain in weight was 10.5 ounces (297.67 Gm.). There was an investigation of 200 normal babies to ascertain how soon

TABLE 7.—*Prognosis in Cases of Fever*

Gain in weight.....	200 Normal cases	9.4 oz.	224 Fever cases	10.5 oz.
Regained birth weight.....	200 Normal cases	65%	224 Fever cases	45%
Deaths.....	4			

they regained their natal weight; it was found that 65 per cent regained it during the first two weeks of life. Only 45 per cent of the 224 patients with fever regained their natal weight. This apparently contradicts what has just been said regarding the gain in weight in ounces for normal infants. It must not be forgotten that the loss of weight in these babies is 2.6 per cent less than the loss in those who had fever; therefore the infants with fever had to gain more in order to regain their first weight than the normal children. Of the 224 cases of fever, four of the babies died.

TREATMENT

The treatment of new-born infants who have fever depends on the etiology; treatment should be given for the individual disease that is causing the fever. In dehydration fever, the treatment for the actual condition consists in giving extra water or extra food in a suitable milk mixture by mouth. Breast milk is preferable. Full supervision of the baby nursing its own mother is important. Colonic flushings are helpful.

The bacteriologic work was done by Dr. Claude P. Brown and his trained technicians. Several methods of obtaining the cultures were tried, but as they all yielded practically the same results, only the present technic is quoted:

The babies were all examined during the first twenty-four hours. The anus and adjacent skin were painted with 1 per cent mercurochrome-220 soluble. A sterile speculum was inserted into the rectum, and cultures were taken through it. Direct plating was done.

SUMMARY

1. Fever in the new-born is of frequent occurrence.

2. There is no apparent relation between its occurrence and excessive summer heat.

3. It is of about equal frequency in babies of multiparous and of primiparous mothers.

4. There is a distinct relation between excessive loss of weight and occurrence of fever.

5. Processes of immunity of the child and bacterial invasion are important factors.

6. Helping the baby secure its full quota of breast secretion, both colostrum and breast milk, in the first few days of life appears to be the best means of preventing fever.

THE ICTERUS INDEX IN CHILDREN*

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Because of the work of Mann and his associates, it is now known that the parenchymal cells of the liver serve to excrete bilirubin but not to form it. The demonstration of this fact supplies the key to many riddles. Bilirubin is formed from the pigment of broken-down red blood corpuscles, and is carried in the blood stream to the liver and there excreted. The amount of bilirubin in the blood at any one time serves as a measure both of the destruction of blood and of the function of the liver.

Various methods for determining the quantity of bilirubin in the blood have been devised, but it was not until Davis, working in the Boston City Hospital, published a paper on "The Determination of the Icterus Index with Capillary Blood" [1] that a practical method for determining the quantity of bilirubin in the blood of infants and small children was available. The method consists in the matching of the patient's serum with standard solutions of potassium bichromate. A serum, the color of which matches a solution of potassium bichromate of from 1 to 10,000 strength is said to represent an icterus index or bile index of 1; one which matches a dilution of from 2 to 10,000, an index of 2; from 3 to 10,000, an index of 3, and so on.

Davis calls attention to certain sources of error in making the determination. Three of these are of particular importance in infants: The first is hemolysis. This occurred in nearly half the specimens from small infants in this series, and seemed to depend more on some inherent quality of the blood than on the technic used in making the determination. Repeated specimens from certain infants would show hemolysis, while from others the serums would always be clear. Recently I learned from Dr. Altnow that hemolysis could be largely prevented if the tube containing the blood was placed immediately in the refrigerator and kept there until the clot had formed and the serum separated, or if the tube was surrounded with a pledget of cotton soaked in ether. Specimens showing even the slightest trace of hemolysis cannot be read and must be discarded. The other two sources of error are easily prevented;

* Received for publication, June 29, 1927.

* Read before the American Pediatric Society, May, 1927.

1. Davis, D.: Determination of Icterus Index with Capillary Blood, Am. J. M. Sc. **172**:848 (Dec.) 1926.

the one is lipemia and it, like the other, carotinemia, can be avoided by taking the blood when the subject is in the fasting state.

As in health there is a constant breaking down of red blood cells with a consequent constant formation of bilirubin, it follows that, normally, a small quantity of bilirubin exists in the blood serum, and this has been found to be constant for the same person. In general, the normal bilirubinemia of the adult is represented by a bile index of 5 or 6, and is lower than this only in cases of secondary anemia in which, with no increased rate in the destruction of blood, there is a diminished amount of hemoglobin available for conversion into bilirubin. Jaundice is not recognizable in the adult and bile pigment does not spill over into the urine with an index lower than 15. The bilirubinemia represented by indexes greater than the normal maximum of 6 and less than 15 is called "latent jaundice."

My interest in this problem grew from my previous studies on the function of the liver in celiac disease. I had observed that the stools in patients with celiac disease and in infants with certain forms of diarrhea due to parenteral infection were paler than was accounted for by the diet which the patient was taking, and I had been anxious to find some way of determining whether or not bile pigment in these cases was excreted through the liver at the normal rate. So far I have been able to make eighty-five satisfactory determinations on seventy different patients. The determinations have all been in duplicate; ten were made on babies under 2 weeks of age, forty-four on infants under 2 years, and thirty-one on children from 2 to 10 years of age. The first thing that became apparent was that after the new-born period is passed, normal infants and children show a lower index than does the adult. A bile index of 2 is common in infants in the first half year of life, and few of the older children showed a bile index above 4. A bile index above 5 was not shown by any patient free from symptoms of disease of the blood or of the liver. The relatively low bile index of normal infants and children is almost certainly associated with the relatively low hemoglobin content of their blood.

Unfortunately, I have not had patients with celiac disease since I began the study, but in two former patients who are now free from symptoms, the index was normal.

The bile index was determined one or more times on seven patients with acute digestive disturbance:

The first was a girl, aged 20 months. The index taken on the second day of an acute infectious diarrhea with green slimy stools was 8. One month later with the child in her usual health, the index was 2.

The second case was that of a girl, aged 18 months. The index taken on the third day of an infectious diarrhea with chalky stools, was 8.

The third patient was a baby, aged 5 months. The index taken on the third day of an infectious diarrhea was 4.

The fourth patient was likewise a baby, aged 5 months. He was suffering with an infectious diarrhea, and the stools were light colored. The index was 4.

The fifth case was that of an infant, aged 10 months, who had diarrhea with pale, foul stools. The index was 5; four days later when he was convalescent, the index was also 5.

The sixth case was that of a boy, aged 18 months. He had been vomiting, and his stools were loose and chalk colored. The index in this case was 8.

The seventh patient was 6 years of age. The color of her stools was normal. She vomited and had abdominal pains. The index was 9. One day later it was 7, and a month later it was 4, which was apparently her normal.

None of these patients had recognizable jaundice.

These results indicate that latent jaundice complicates an uncertain proportion of the indigestions of infancy due to parenteral infections, but in only two of the four cases in which the bile index was raised were the stools noticeably paler than normal.

A mild grade of icterus frequently occurs in pneumonia, and Bernheim, who investigated the matter, found that the degree of latent jaundice as determined by the bile index was of value in prognosis. Her observation was that no case in which the patient had an index below 7.5 ended fatally. I was surprised to find indexes below 6 in each of the three patients with lobar pneumonia on whom I was able to make a determination. In one of these the disease resulted fatally. Nevertheless, in this case the test was of diagnostic if not of prognostic value. The infant, 9 months of age, was brought into the office because of prostration, diarrhea and vomiting. The temperature was 104.4 F.; the white blood cell count was 25,000; the red blood cell count 2,440,000, and the hemoglobin 38 per cent. The results of physical examination were negative, but the fluoroscope showed a small shadow to the right of the heart. The bile index was 2; this ruled out the possibility of an acute hemolytic anemia. Subsequently, the infant developed all the typical signs of lobar pneumonia of the right lung.

In a second instance, likewise, the test was of diagnostic importance.

A girl, aged 6 years, on the evening of March 16, had three loose stools. On the morning of March 17 she was taken with sharp pain in the abdomen and when seen, had a definite rigidity of the right rectus muscle. The white blood cell count was 17,000 with 81 per cent polymorphonuclears. The urine was normal. She was examined by a conservative surgeon who considered the case to be one of acute appendicitis, and advised operation. A bile index was made and found to be over 9. On the basis of this observation, the operation was postponed. Later in the day, a positive Gmelin test was obtained on the urine. Next day the leukocyte count had dropped to 9,000; the bile index was between 7 and 8, and she was definitely improved. Further bile was not found in her

urine, and at no time was she manifestly jaundiced. Her stools were never clay colored. She made an uninterrupted recovery. One month later, her bile index was 4.

The diagnosis in this case was doubtful, but it certainly was not acute appendicitis. Nevertheless, a laparotomy would have been performed if the bile index had not been taken.

Determinations were made on ten infants in the new-born period. They varied from 2 to 14 days in age, and the bile index—whether or not the baby appeared to be jaundiced—was never below 20. I was able to redetermine the index on two of these babies later. In one, at the age of 23 days, the index was 8. In another, at the age of 1 month, the index was 4. How long the bile index remains raised in full term babies has not yet been determined. I was interested in watching the index in three premature infants. In one, at the age of 1 month, the index was still 50; at 6 weeks, it was 75; at 7 weeks, it was 50; at 2 months, it was 20, and at 9½ weeks, it was 15. A second baby, who was only slightly premature, had a bile index of 50 at the age of 2 weeks, and at 6 weeks the bile index had fallen to 12. The third premature infant had a bile index of 50 at the age of 1 month.

Before determining the index in these small infants, I made a note as to whether or not the baby was jaundiced. As a rule, my note was to the effect that the child was not jaundiced; the bile index would then be determined and would be found to be greater than 20, which indicated a degree of jaundice which should have been manifest clinically.

Thinking that the delayed lowering of the bile index in premature infants might be significant of an increased destruction in the blood which could cause the anemia that so regularly develops in these babies, I had red blood cell counts and hemoglobin determinations made parallel with determinations of the bile index. My figures so far are inconclusive. The premature baby whom I followed the longest had a bile index of 75 at the age of 6 weeks (which was the time of the first red blood cell count), a red blood cell count of 3,010,000 and a hemoglobin content of 60 per cent. At 9½ weeks, the bile index had fallen to 15, the hemoglobin was 65 per cent, and the red blood cell count was 3,340,000. Parallel blood counts, determinations of hemoglobin, and determinations of bile index will have to be made from birth on, both on premature and full term infants to settle this point.

COMMENT

The conclusion can be drawn that in infants born prematurely the bile index remains high for weeks or even for months after manifest icterus neonatorum has disappeared. The normal index which is then reached is definitely lower than the normal index for the adult.

Determinations of the icterus index provide a method for studying the function of the liver in infants and in children and for furthering an understanding of the nature of some forms of indigestion and diarrhea. Such determinations may help to elucidate the nature of certain types of anemia in infancy, and from time to time will be of decided diagnostic importance. They will distinguish hemolytic from secondary anemia. They will, as in the case quoted, help to make the diagnosis between appendicitis and disease of the biliary tract, and will serve as the best method of determining whether a manifest jaundice is increasing or diminishing.

SEASONAL VARIATION IN THE CALCIUM CONTENT OF INFANTS' SERUM *

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It is well known that tetany in infants shows a striking seasonal incidence. The condition is rare during the summer and autumn months, but is common in the winter and particularly in the spring. As infantile tetany is associated with a diminution in the calcium content of the serum, it seemed of interest to determine whether a fluctuation in the serum calcium of infants at various times of the year is physiologic. A seasonal tide has been demonstrated by Hess and Lundagen [1] for the inorganic phosphorus of infants' blood, corresponding to the increased incidence and severity of rickets during the winter and spring months. Grant and Gates [2] have observed fluctuations in the serum calcium concentration of rabbits with low values in January and with high values in May and November.

The infants whom we studied ranged in age from 3 to 24 months, but most of the observations were made on infants between 6 and 18 months. Sick as well as healthy babies were included, only those with nephritis being excluded. The serum calcium was estimated by the Clark-Collip [3] modification of the Kramer-Tisdall method,[4] 2 cc. of serum being used. The original Kramer-Tisdall method was used for turbid serums.

In chart 1 the results of individual determinations made during 1926 and during the first three months of 1927 are shown. The lightly drawn dotted lines represent the approximate limits within which the majority of determinations are massed. The chart shows clearly the rise and fall in the calcium of infants' serum at various seasons of the year. There is a gradual drop in the values from January to March,

* Received for publication, July 26, 1927.

* From the Department of Diseases of Children, College of Physicians and Surgeons, Columbia University; the Children's Medical Division and Department of Pathology, Bellevue Hospital.

1. Hess, A. F., and Lundagen, M. A.: A Seasonal Tide of Blood Phosphate in Infants, J. A. M. A. **79**:2210 (Dec. 30) 1922.

2. Grant, J. H. B., and Gates, F. L.: Some Factors Affecting the Levels of the Serum Calcium and Phosphorus of Normal Rabbits, Proc. Soc. Exper. Biol. & Med. **22**:315, 1925.

3. Clark, E. P., and Collip, J. B.: J. Biol. Chem. **63**:461, 1925.

4. Kramer, B., and Tisdall, F. F.: J. Biol. Chem. **48**:223, 1921.

after which the rise starts and continues into the summer months. Determinations were not made during July, August or September, but in October, when the work was again taken up, the serum calcium level was much higher than during the preceding June. The autumnal drop in the wave could be observed in November. It continued to

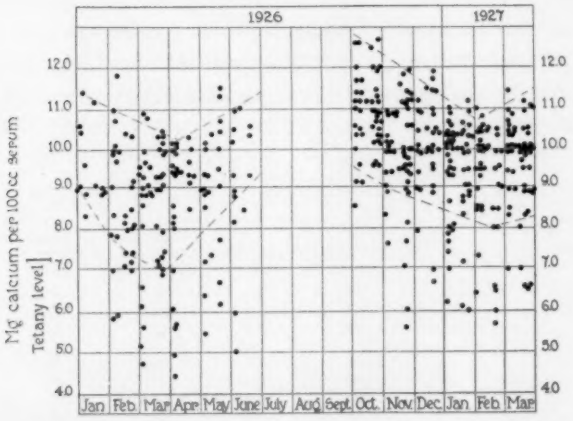

Chart 1.—Seasonal variation in the serum calcium of infants. The dots represent individual determinations.

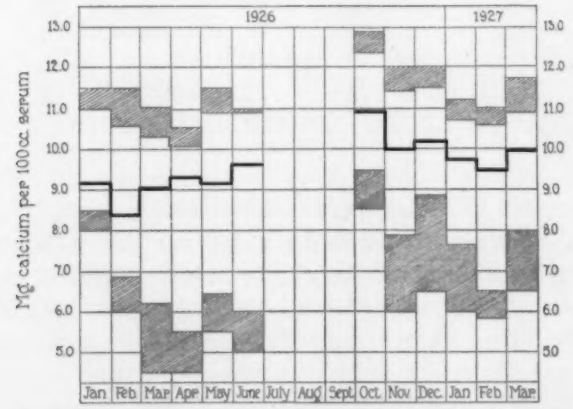

Chart 2.—Seasonal variation in the serum calcium of infants. The heavy line represents the medians for the various months; the upper and lower cross-hatched areas, the uppermost and lowermost 10 per cent of all determinations for each month.

fall, but remained at a slightly higher level than during the corresponding months of the preceding year. The spring rise began somewhat earlier. The seasonal fluctuation in the serum calcium is illustrated by another method in chart 2. The heavy solid line represents the

medians for the various months, the upper and lower cross-hatched areas the uppermost and lowermost 10 per cent for each month. It is apparent from both charts that the low level during the winter and spring months is not due to the inclusion of many infants with tetany, but represents a real flux in the serum calcium of the infant.

The curve for the serum calcium shows a striking parallelism with that described by Hess and Lundagen [1] for the inorganic phosphorus content of infants' blood. These observers attribute the variations in the phosphorus to the seasonal fluctuations in the ultraviolet radiation of the sun.

Meteorologic Data for New York City

1925	Actual Sunshine, Hours	Cloudiness	Mean Relative Humidity	Mean Temperature	Total Precipitation
October	193	6.6	63.8	50.6	4.52
November	184	5.5	63.0	43.9	2.93
December	168	5.7	66.0	34.8	3.30
1926					
January	162	6.6	62.5	32.0	2.85
February	164	6.5	66.9	29.2	5.37
March	274	4.6	57.6	35.7	2.66
April	281	5.9	54.3	47.3	1.73
May	346	3.8	55.5	60.0	2.42
June	288	6.0	63.0	66.8	1.71
July	356	5.5	67.3	75.0	6.38
August	256	6.6	78.4	74.0	7.28
September	247	5.5	74.2	65.6	4.78
October	182	6.0	70.3	55.0	4.87
November	182	5.6	68.0	44.9	3.78
December	164	5.9	66.6	28.8	4.00
1927					
January	163	6.0	66.7	30.9	2.03
February	185	6.3	68.2	36.4	3.46
March	210	6.0	62.3	42.6	2.05

Meteorologic data for New York City during the last three months of 1925, the year 1926 and the first three months of 1927 are shown in the table. These were obtained through the United States Department of Agriculture. The relative amounts of ultraviolet radiation in the sun's spectrum at various times of the year have been determined by Dorno,[5] at Davos, Switzerland. He obtained minimal values between November and March; a sharp rise started in April and reached a maximum in June and July, after which the ultraviolet radiation decreased. Such data are not yet available for New York City.

The median values for the serum calcium follow in a general way the figures for the ultraviolet radiation. This does not necessarily imply a direct relationship, but the fact that low serum calcium values in an infant with tetany can be raised to normal within from ten to twenty

5. Dorno: Physic der Sonne und Himmelstrahlung und Klimatologie im Dienste der Medizin, 1920.

days by exposure to ultraviolet radiation [6] from artificial sources, renders it probable that the variation in the ultraviolet content of the atmosphere at different times of the year is a factor in determining the seasonal fluctuations of the serum calcium.

Other meteorologic conditions may also have an influence. Riesenfeld, Handelman and Rose [7] believe that humidity is of importance in regulating the seasonal variations of the inorganic phosphorus of infants' blood. They hold with Dobson [8] that increased humidity and precipitation wash out from the atmosphere dust or particles which, under ordinary circumstances, act as a filter to the ultraviolet radiation of the sun.

Outside temperature also has its influence, the warm days permitting greater exposure to the ultraviolet radiation of the sun, the cold days prohibiting it. Thus such meteorologic factors as humidity, precipita-

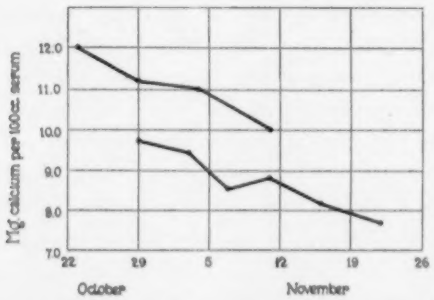

Chart 3.—Drop in the level of the serum calcium of two infants with febrile infection. The curves represent, respectively, the levels of the serum calcium of two infants over a period of about three weeks.

tion and outside temperature seem of importance so far as they permit the child to obtain more or less of the ultraviolet radiation of the sun.

Another seasonal factor which as yet cannot be directly linked with variations in the sun's ultraviolet radiation is the frequency of infections during the winter and spring months. In chart 3, the influence of a

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6. Hess, A. F.: Newer Aspects of Rickets Problem, J. A. M. A. **78**:1177 (April 22) 1922. Hoag, L. A.: Treatment of Infantile Tetany with Ultraviolet Radiation, Am. J. Dis. Child. **26**:186 (Aug.) 1923. Casparis, H., and Kramer, B.: Bull. Johns Hopkins Hosp. **34**:219, 1923.

7. Riesenfeld, E. A.; Handelman, I., and Rose, A. R.: The Inorganic Phosphorus in the Blood of the New-Born, Am. J. Dis. Child. **30**:646 (Nov.) 1925.

8. Dobson, G. M. O.: Measurement of the Sun's Ultraviolet Radiation and Its Absorption in the Earth's Atmosphere, Proc. Roy. Soc. London, Ser. A. **104**: 252, 1923.

prolonged febrile infection (acute miliary tuberculosis) on the serum calcium of two infants is illustrated. In both patients, represented by the respective curves, there is a fall in the serum calcium amounting to 2 mg. over a period of about three weeks. Such changes have been found to be of frequent occurrence in infants with fever, and, although occasionally seen in hospitalized infants without fever, they are not ordinarily so rapid.

The values for the first three months of 1926 and 1927 may be compared in charts 1 and 2. In 1927, the level was considerably higher than during the same period in 1926, and the rise in the serum calcium began earlier; also the tetanic values for 1927 were not so low as those for 1926. These differences correspond to the more favorable weather conditions during February and March of 1927 and to the smaller number of febrile infections during that period. In December, 1925, and in January, February and March, 1926, sixty-four infants under 2 years of age were admitted to the wards of Bellevue Hospital with pneumonia, while during the corresponding months of the following year only thirty-nine patients with the same ailment were admitted.[9] We have chosen pneumonia as an index for the frequency of infections in infants, because febrile hypocalcemia seems to occur most readily with respiratory disease,[10] and because it is one of the commonest seasonal infections in which the patient's temperature is sustained.

A clue to the mechanism by which ultraviolet radiation raises the serum calcium may be found in the work of Grayzel and Miller.[11] These observers found that exposure to ultraviolet radiation lowers the intestinal p_H in dogs, thus, presumably, favoring absorption of calcium. However, cod-liver oil has a similar influence on the intestinal p_H of dogs, but has no constant effect on the serum calcium of infants. The change in the weight of the parathyroid glands following exposure of rabbits to ultraviolet light[12] probably also has a bearing on the mechanism of the fluctuations in serum calcium at various seasons of the year.

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9. According to the Weekly Bulletin, City of New York, Department of Health **16**:86, 1927, there were only one hundred and five deaths due to bronchopneumonia during the first sixteen weeks of 1927 as compared with two hundred and twenty-six during the same period in 1926.

10. Peabody, F. W.: Studies of the Inorganic Metabolism in Pneumonia with Special Reference to Calcium and Magnesium, J. Exper. Med. **17**:71, 1913.

11. Grayzel, D. M., and Miller, E. G.: p_H Concentration of Intestinal Contents of Dogs with Special Reference to Inorganic Metabolism, Proc. Soc. Exper. Biol. & Med. **24**:668, 1927.

12. Grant, J. H. B., and Gates, F. L.: Effect on the External Parathyroid Glands of the Exposure of Rabbits to Ultraviolet Light, J. General Physiol. **6**: 635, 1924.

SUMMARY

1. The serum calcium of infants shows a definite seasonal variation, the drop beginning during the autumn, reaching the lowest point during the early spring months and then rising as summer approaches.

2. At least two factors are responsible for these fluctuations: the seasonal variation in the amount of available ultraviolet radiation of the sun and the large number of infections during the winter months.

THE ESTIMATION OF RENAL EFFICIENCY OF CHILDREN

STUDIES ON THE EXCRETION OF NITROGEN *

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AND
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Though clinical methods at present available for the study of the function of the kidney are not entirely satisfactory, one does, by a combination of certain tests, obtain a fairly reliable index of the renal efficiency of adults. The selection of tests from the many available depends chiefly on clinical ideas of lesions of the kidney. It may be said, generally, that there are three types of tests: (*a*) those detecting and measuring disturbances of the excretion of nitrogen, (*b*) those showing disturbances in the excretion of salt and of water, and (*c*) those indicating the efficiency of the kidneys in the part they play in regulating body neutrality. In the present communication we are concerned chiefly with the first type of test, namely, that which indicates the efficiency of the kidneys in the excretion of nitrogen.

The general principle underlying the various tests in use is that when the kidneys are not able to excrete a normal end-product of protein metabolism, it either must be excreted more slowly than normally, or must accumulate in the blood stream, and the rate of its excretion in the urine or the degree of its retention in the blood is an index of the degree of impairment of renal efficiency.

The importance of the selection of a suitable end-product for study is obvious. The ideal choice is a substance normally excreted by the kidneys. Its physiology should be reasonably well known, and in order to excrete it, the kidneys should do a great amount of work. From the time of ingestion to that of excretion it should not undergo any chemical alteration. Extrarenal factors during its excretion should be reasonably well controlled, and for its determination technical difficulties should be at a minimum. In a previous communication one of us (I. M. R.) has shown [1] that urea is an ideal substance for such a study, since it complies with the foregoing requisites. Urea is a normal end-product of protein metabolism, and in the average adult on an average diet, it

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* From the Laboratory of the Shriners' Hospital for Crippled Children.
* This work was done with the aid of a Grant from Mr. Henry J. Elliott, K. C.

1. Rabinowitch, I. M.: The Urea Concentration Factor in the Estimation of Renal Efficiency, Arch. Int. Med. **32**:927 (Dec.) 1923.

constitutes about from 80 to 90 per cent of the total nitrogen eliminated in the urine in twenty-four hours. Unlike some other urinary constituents, a great deal of work must be done by the kidney in excreting urea; this energy can be calculated according to known physical principles by applying the Vant Hoff theory of solutions. Further proof of the great amount of work required of the kidney to excrete urea is furnished by the experiments of Barcroft and Straub on the consumption of oxygen by the kidney in relation to diuresis. There is a marked contrast between these results and those obtained with diuresis due to Ringer's solution, water or sodium chloride. Urea is uniformly distributed in all the organs and tissues of the body, including the blood.[2] An appreciation of this fact is important. The uniform diffusion of urea prevents differences in osmotic pressure across the membranes of the body. Hence, this absence of differences in osmotic pressure will not influence the movement of the body fluids and will therefore be less likely to cause hydremia,[3] which is an important factor influencing renal excretion. Following the administration of urea, it does not undergo a chemical change, and normally its rate of elimination is rapid. When prevented from being excreted, it is all stored in the body, with the exception of traces which appear in the bile and sweat. Its rate of excretion is governed partly by its concentration in the blood. Diuresis following the administration of urea is due to the activity of the kidneys alone. Large amounts may be injected and followed by considerable diuresis; yet there may not be any increase in the flow of blood through the kidneys. This is demonstrated in one of the experiments by Lamy and Mayers.[4] Besides the fact that excretion of urea is chiefly a function of the kidneys, extrarenal factors such as those causing high or low cencentrations of urea in the blood are more easily accounted for than factors which influence other tests.

The three methods of studying urea generally in use are: (*a*) determination of its concentration in blood, (*b*) determination of its concentration in urine following ingestion of urea and (*c*) determination of the relationship between its concentration in the blood and either its concentration or the rate of its excretion in urine. In a comparative study of these three procedures,[5] one of us (I. M. R.) has mentioned some of the many variables which must be considered in the interpretation of observations made by the first two methods. For example, conditions other than altered renal activity may result in high concentrations

2. Marshall, E. K., and Davis, D. M.: Urea, Its Distribution and Elimination from the Body, J. Biol. Chem. **18**:53, 1914.

3. Dresser, in Cushny, A. R., Monograph in Physiology. The Secretion of Urine, New York, Longmans, Green & Company, 1917.

4. Lamy and Mayers, quoted by Cushny: J. Physiol. & Path. **8**:258, 1908.

5. Rabinowitch, I. M.: A Quantitative Index of Kidney Function, Arch. Int. Med. **34**:365 (Sept.) 1924.

of urea in the blood (acute pancreatitis, general peritonitis, intestinal obstruction and epidemic encephalitis), and the concentration of urea in urine may be influenced by other than renal factors (volume of output of urine, blood urea concentration and others). It was shown that, at least so far as lesions associated with defective excretion of nitrogen are concerned, the last type of the aforementioned tests was of greater value than others used for the same purpose. The three tests generally in use and belonging to this type are (*a*)
Addis' ratio:

$$\frac{\text{urea in one hour's urine}}{\text{urea in 100 cc. of blood}}$$

(*b*) Van Slyke's "urea secretory constant":

$$\frac{D}{B\sqrt{VW}}$$

when D = grams urea per twenty-four hours
V = liters urine per twenty-four hours
W = body weight and
B = grams urea per liter of blood

and (*c*) the "urea concentration factor":

$$\frac{\text{Mg. urea per 100 cc. of urine}}{\text{Mg. urea per 100 cc. of blood}}$$

of Harrison.

Of the three methods just described, we have confined our studies in this investigation to the "urea concentration factor" and the "urea secretory constant." The reliability of the "factor" when performed under the set of conditions described [1] has been proved by one of us (I. M. R.) [6] by comparing data concerning it with those of Van Slyke's "urea secretory constant" which take into consideration extrarenal factors, such as volume of output of urine. This was shown in three ways.

First, values for the "factor" and "constant" were obtained in the same persons. Twenty normal subjects and forty patients with albuminuria were included in this study. The normal and pathologic cases were grouped separately. A statistical study was made of the normal group. The arithmetical means, standard deviations and coefficients of variation were calculated. The forty cases of albuminuria were divided into five groups according to the "factor" values. Thus group 1 consisted of factors from 41 to 50, group 2 consisted of those from 31 to 40 and so on. In each group the value of the mean of the corresponding "constants" was found. The "factors" and their corresponding constants (mean values) of the different groups of albuminuria are shown in table 1. Second, the means standard devia-

6. Rabinowitch, I. M.: Urea Tests of Renal Efficiency, J. Biol. Chem. **65**:617, 1925.

tions and coefficients of variation were calculated both for this "factor" and for the "constant" for the normal subjects. These are shown in table 2. Lastly, the observations in a case previously cited [6] in illustration of (*a*) the parallelism between the "factor and constant," and (*b*) between the latter and the clinical picture are here reproduced.

A man, aged 27, was admitted to the Medical Service of Dr. A. H. Gordon, with a diagnosis of acute nephritis. The complete laboratory data are shown in table 3.

TABLE 1.—*The Factors and Corresponding Constants in Five Groups of Patients with Albuminuria*

Group Number	"Factor"	"Constant"
1	41 to 50	6.3
2	31 to 40	4.5
3	21 to 30	3.1
4	11 to 20	2.7
5	1 to 10	1.0

TABLE 2.—*Showing the Standard Deviation and the Coefficients of Variation for the Normal Subjects*

Test	Mean Value	Standard Deviation	Coefficient of Variation
Urea secretory constant	9.8	±1.4	14.3
Urea concentration factor	47.3	±6.9	14.6

TABLE 3.—*Clinical Observations on Patient with Acute Nephritis*

Date	Weight, Kg.	Blood Urea Nitrogen: Before Urea, Mg. per 100 Cc.	Blood Urea Nitrogen: After Urea, Mg. per 100 Cc.	Urine Second Hour Specimen: Volume, Cc.	Urine Second Hour Specimen: Urea, per Cent	U/B (Factor)	D/BV/W (Constant)	Comment
June 9	65.4	38	46	60	1.51	16.9	2.6	
June 14	65.7	34	43	55	1.44	17.4	2.5	
June 19	65.0	35	41	85	1.24	15.2	2.7	
July 4	64.7	28	42	105	1.60	21.3	4.2	No edema; blood disks still present in urine
July 15	64.0	24	31	95	0.94	14.2	3.0	No edema; blood disks still present in urine
July 21	64.6	22	27	70	0.96	18.3	2.9	No edema; blood disks still present in urine
July 28	64.6	21	37	95	2.76	44.4	8.3	No blood disks in urine
Aug. 2	62.5	21	32	40	2.28	40.2	5.5	No blood disks in urine
Aug. 8	61.8	22	35	45	2.76	45.2	6.0	No blood disks in urine

A low factor and a low constant are noted during the acute stage of the illness. During the stage of convalescence, they approach the normal values. Until July 21, though the patient had appeared to be well for over two weeks previously, there was no alteration either of the "factor" or of the "constant." The only evidence of disease clinically was the persistence of isolated red blood cells in the urine. Following the disappearance of the blood from the urine, both the "factor" and the "constant" increased in value. A parallelism between the clinical picture and the factor, and between the factor and the constant is thus noted.

Some idea of the sensitivity of the "urea concentration factor" when the test is performed under the proper set of conditions may be had from the following observations previously recorded.[5] Of 610 observations made on 284 patients with albuminuria, the blood urea was the least sensitive in detecting early renal efficiency, having been found increased in 341, or only 56 per cent, of the total number of observations. The concentration of urea in the urine was a better index than the urea values of the blood that were below normal, having been found in 453 or 76 per cent of the total number of observations. The "urea concentration factor" was the most sensitive, showing impairment in 573 or 94 per cent of all the observations; the reason for this appears to be obvious. The earliest evidence of impaired function is usually a diminution in the ability of the kidneys to concentrate, but by constant effort, the total end-products of protein metabolism may be eliminated during a day. Under these conditions, the concentration of urea in the blood will be normal in the postabsorptive state on the following morning. The test for the concentration urea is the urine would thus be more sensitive than that for the concentration of urea in the blood. The reasons why the "urea concentration factor" is the most sensitive have been discussed in a previous paper.[1]

Briefly, the "urea concentration factor" is obtained as follows: No food or fluids are allowed after 6 o'clock on the evening before the test. At 6 o'clock on the morning of the test, the patient voids. This specimen is discarded. Fifteen grams of urea dissolved in 150 cc. of water are then given orally. No food or fluids are allowed during the test. Blood is collected for analysis before and two hours after the test, and the urine one and two hours after the administration of the urea. Determinations of urea are made on the blood and on the urine by the Van Slyke (urease) method. All determinations are made in duplicate. The "urea concentration factor" is calculated according to what was subsequently [5] shown to be a more exact method than that first employed, in that the average of the value of the urea content of blood taken before and after administration of urea is used instead of the original specimen.

Thus:

$$\text{Urea concentration factor} = \frac{U}{\left(\frac{(a+b)}{2}\right)}$$

when U = mg. urea per 100 cc. of urine (second hour specimen)
a = mg. urea per 100 cc. of blood before giving urea
b = mg. urea per 100 cc. of urine of blood after giving urea

A series of observations were made on fifty children in order to determine whether the test might be used for them. They were all patients with various orthopedic conditions, but, as far as could be ascertained from their histories and the clinical observations, their kidneys

were normal. In each case, however, the urine was tested and found to be clear; it did not contain albumin, casts, pus, blood or bacteria. In view of the fact that little is known of the rate of excretion of urea in urine in children, body weight and volume of output of urine were

TABLE 4.—*Relationships of Concentrations of Blood Urea to Concentrations of Urine Urea of Fifty Children*

Subject	Sex	Age	Weight, Kg.	Blood Urea Nitrogen, Mg. per 100 Cc.		Urine Second Hour After Ingestion of Urea		$\frac{U}{B}$	$\frac{D}{B\sqrt{VW}}$
				Before Giving Urea	After Giving Urea	Volume, Cc.	Per Cent of Urea	"Urea Concentration Factor"	Secretory Constant
1. K. P.	M	6	18.8	15.4	39.2	19	2.41	39.9	6.4
2. V. W.	M	13	35.6	14.0	31.0	11	2.44	65.2	5.6
3. W. L.	M	14	33.8	8.4	24.5	75	1.62	46.0	11.5
4. R. S.	M	13	29.0	14.0	29.4	47	2.59	55.8	11.0
5. D. M.	F	10	26.8	11.2	28.0	66	2.38	56.7	13.8
6. L. B.	F	10	33.6	11.2	25.2	55	2.43	62.4	12.3
7. O. P.	F	13	27.9	12.6	18.2	100	1.26	38.2	11.2
8. R. P.	M	12	32.2	11.2	25.2	51	2.48	63.7	12.4
9. E. B.	F	11	40.9	18.2	20.0	29	3.60	72.8	9.5
10. H. M.	M	..	17.7	15.4	40.6	47	3.00	50.0	12.7
11. P. D.	M	13	37.9	21.0	35.0	39	3.25	54.3	8.5
12. G. B.	M	13	30.4	16.8	30.8	66	2.25	44.1	10.1
13. Z. B.	M	10	20.4	11.2	28.0	28	2.95	70.3	12.7
14. N. S.	F	6	16.8	16.8	29.0	85	2.92	59.6	20.6
15. M. F.	M	5	14.5	16.8	42.0	67	2.76	43.9	14.8
16. R. T.	F	12	30.9	9.8	19.6	61	2.88	91.6	20.0
17. R. S.	M	12	28.1	7.0	16.8	45	2.22	87.4	17.1
18. T. M.	F	11	26.8	12.6	28.0	70	3.40	78.3	19.6
19. H. E.	M	5	16.8	9.8	26.6	35	3.02	77.5	17.3
20. M. M.	M	12	25.2	16.8	36.4	70	3.55	62.3	16.1
21. F. H.	F	10	29.0	15.4	29.4	58	2.40	50.0	10.9
22. F. D.	F	14	34.7	8.4	16.8	75	2.55	94.7	21.6
23. F. M.	F	14	48.1	18.2	30.8	80	2.62	49.9	9.9
24. E. T.	M	10	23.6	14.0	33.6	114	2.60	51.0	17.4
25. G. .V	M	13	35.0	14.0	30.8	30	2.91	60.7	8.7
26. M. P.	F	13	27.7	14.0	22.4	31	2.52	64.7	10.6
27. F. M.	F	14	48.1	18.2	30.8	80	2.62	49.9	9.9
28. E. T.	M	10	23.6	14.0	33.6	114	2.60	51.0	17.4
29. M. C.	F	9	20.7	15.4	14.0	83	0.84	26.7	8.2
30. R. P.	M	10	42.2	14.0	26.6	40	3.55	81.7	12.3
31. G. Y.	M	13	35.0	14.0	30.8	30	2.91	60.7	8.7
32. M. P.	F	13	27.7	14.0	22.4	31	2.52	64.7	10.6
33. W. W.	M	11	29.5	15.4	42.0	54	2.22	36.1	7.6
34. A. R.	F	10	39.7	16.8	2.80	63	2.76	57.6	11.2
35. M. T.	F	8	18.4	16.8	33.6	90	0.96	17.8	5.8
36. G. T.	M	14	39.3	23.8	35.0	50	3.84	61.0	10.6
37. J. H.	M	8	16.5	11.2	37.8	110	2.20	41.9	16.7
38. H. L.	M	11	27.0	11.2	19.6	52	2.26	68.6	14.8
39. B. A.	M	6	17.0	8.4	42.0	190	2.70	60.0	25.9
40. H. N.	M	10	22.5	9.8	35.0	40	2.55	53.2	10.7
41. I. N.	M	5½	18.1	14.0	49.0	25	3.22	46.0	8.7
42. L. L.	F	14	40.4	16.8	19.6	50	3.33	82.5	14.6
43. R. M.	M	12	25.0	12.6	18.2	20	3.07	98.2	12.9
44. A. C.	M	13	28.1	16.4	33.6	54	3.11	58.1	12.5
45. G. M.	F	13	36.3	22.4	28.0	64	3.12	57.9	11.9
46. H. S.	F	8	23.6	14.0	30.8	116	2.40	50.1	16.9
47. F. S.	F	9	18.6	12.6	32.2	50	2.40	50.1	12.7
48. F. H.	M	12	29.0	11.2	22.4	25	2.98	82.9	11.9
49. M. S.	M	9	22.5	15.4	32.2	52	3.16	62.0	14.6
50. R. P.	M	10	42.2	14.0	26.6	40	3.55	81.7	12.3
Average								59.5	12.8
Standard deviation								±15	±4
Coefficient of variation								25	31

taken into account, and thus in each case it was possible to calculate the Van Slyke's "urea secretory constant."

The only modification of the test was that 10 Gm. of urea was given instead of 15 Gm., the amount given to adults. The combined data are shown in table 4.

COMMENT

It is interesting to note (column 7) that, unlike adults, the polyuric response to ingestion of urea in children was uncommon. Of the fifty cases, the volume of urine in six instances was 100 cc. or more (nos. 7, 24, 28, 37, 39 and 49); in only one case (no. 39) was there a definite polyuric response, namely, 190 cc. of urine.

As would be expected, the increase in the concentration of urea in the blood following ingestion of urea was greater than in adults. The average increase in adults was 9 mg.,[1] whereas in the children it was 14.7 mg. per hundred cubic centimeters.

The average "urea concentration factor" (column 9) was 59.5 with a standard deviation of $\pm$ 15 and a coefficient of variation of 25. A better idea of its clinical value may be had, however, by comparing the results of the "factor" with those of the "urea secretory constant," as was done with adults. It will be noted (column 10) that the average value of the constant was 12.8 with a standard deviation of $\pm$ 4 and a coefficient of variation of 31.

In view of the proved value of the "urea concentration factor" in the great majority of adults and of the observations in children, it appears that for children this test is a means of determining renal efficiency so far as excretion of nitrogenous substances is concerned.

BLOOD AND CEREBROSPINAL FLUID SUGAR*

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Much uncertainty prevails concerning the changes in the concentration of sugar in the cerebrospinal fluid in disease. This is due in part to the divergence in the results obtained by various observers even with the cerebrospinal fluid of normal persons. Schloss and Shroeder,[1] in their series of cases, found that the concentration of glucose in the cerebrospinal fluid varied from 50 to 134 mg. per hundred cubic centimeters. Wittengstein [2] found from 45 to 60 mg. of glucose per hundred cubic centimeters and obtained high values for the sugar in the spinal fluid of diabetic patients. In the studies of Seham and Nixon,[3] the average amount of sugar in the spinal fluid was 69 mg. per hundred cubic centimeters. In our series of human cases, we also obtained a marked fluctuation, which was between 40 and 194 mg. (table 1).

This marked variation led us to study the subject more closely, in order to define the normal limit more precisely and to determine the factors that mark the extremes. Simultaneous determinations of blood and cerebrospinal fluid sugar were made, but a consistent relationship could not be established (table 1). Wilcox and Lyttle [4] state that normally the cerebrospinal fluid sugar content is about one half of that of the blood. In our cases the ratio of the sugar in the cerebrospinal fluid to the sugar in the blood varied between 40.8 and 82.6 per cent. Seham and Nixon [3] found the sugar of the cerebrospinal fluid to be between 50 and 80 per cent of the sugar in the blood, and Kubie and Schultz [5] noted the reducing substance in the cerebrospinal fluid to be from 33 to 81 mg. per hundred cubic centimeters, and the ratio to vary from 33 to 81 per cent of the concentration of the sugar in the blood.

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* From The Harry Caplin Pediatric Research Laboratory and The Pediatric Department of The Jewish Hospital.

1. Schloss, O. M., and Shroeder, L. C.: Am. J. Dis. Child. **11**:1 (Jan.) 1916.

2. Wittengstein, A.: Nature and Quantitative Determination of the Reducing Substance in Normal and Pathologic Cerebrospinal Fluid, Deutsche med. Wchnschr. **49**: 246, 1923.

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4. Wilcox, H. B., and Lyttle, J. D.: Arch. Pediat. **40**:215, 1923.

5. Kubie, L. S., and Schultz, G. M.: J. Exper. Med. **42**:565, 1925.

PERSONAL OBSERVATIONS ON PATIENTS

We observed that the variation in the concentration of sugar in the cerebrospinal fluid was least in those patients that were starved for a period of ten hours or more. It fluctuated between 40.2 and 75.9 mg. per hundred cubic centimeters. In 82.7 per cent of the cases (table 2)

TABLE 1.—*Blood Sugar and Cerebrospinal Fluid Sugar in Twenty-Nine Fasting Patients, in Order of Number of Milligrams of Glucose Per Hundred Cubic Centimeters of Cerebrospinal Fluid*

Case No.	Name	Sex	Age	Condition	A. Blood Sugar Mg. per 100 Cc.	B. C. S. Fl. Sugar Mg. per 100 Cc.	Ratio B/A per 100 Cc.
14	W. M.	M	1 yr. 10 mos.	Tuberculous meningitis	98.4	40.2	40.8
26	R. S.	F	6 mos.	Mental retardation	75.1	44.6	59.3
1	B.	M	7 yrs.	Tuberculous meningitis	110.0	48.1	42.8
24	R. E.	F	4 yrs. 3 mos.	Mental retardation	87.3	52.6	60.2
16	C. A.	M	3 yrs.	Abdominal neoplasm	81.8	55.0	67.2
17	C. F.	M	15 mos.	Acute tonsillitis	130.8	55.5	42.4
34	M. C.	M	3 yrs. 2 mos.	Lobar pneumonia	90.1	56.0	58.2
6	B. L.	M	3 yrs.	Unexplained convulsions	113.8	58.8	51.6
23	G. B.	F	10 mos.	Unexplained convulsions	82.6	59.0	71.4
30	E. S.	M	11 yrs. 8 mos.	Unexplained convulsions	100.3	60.1	59.9
7	A. N.	F	4 yrs. 6 mos.	Unexplained convulsions	104.8	60.4	57.6
31	O. Y.	M	5 yrs. 10 mos.	Unexplained convulsions	100.1	61.0	60.9
19	R. L.	F	1 yr. 3 mos.	Unexplained convulsions	98.0	61.3	62.5
21	S. P.	M	4 yrs.	Poliomyelitis	110.1	61.3	55.6
20	R. E.	M	4 yrs. 1 mo.	Encephalitis	99.0	61.6	62.2
3	E. R.	M	1 yr.	Cerebral malformation	112.3	63.3	56.3
5	H. B.	M	3 yrs. 10 mos.	Acute tonsillitis	121.5	65.0	53.4
10	P. C.	F	3 yrs. 6 mos.	Mental retardation	122.5	65.5	53.0
13	M. W.	F	12 yrs. 6 mos.	Acute hemorrhagic nephritis	104.9	67.1	63.0
29	B. B.	F	6 yrs. 10 mos.	Sinus thrombosis	109.5	67.1	61.2
25	J. B.	F	27 mos.	Acute tonsillitis	82.2	67.5	82.1
12	H. C.	M	2 yrs.	Acute tonsillitis	105.5	67.5	64.0
9	B. B.	M	2 yrs. 6 mos.	Chronic tonsillitis	102.3	68.4	66.0
18	B. R.	M	6 yrs. 11 mos.	Rhinopharyngitis and cervical adenitis	101.8	68.5	67.2
2	M. S.	M	6 yrs.	Unexplained convulsions	99.8	68.9	68.2
22	P. S.	M	4 yrs.	Encephalitis	105.0	69.0	65.7
37	R. F.	F	8½ mos.	Unexplained convulsions	100.5	69.1	68.7
35	R. R.	F	1 yr. 2 mos.	Primary bronchopneumonia	121.8	70.4	57.8
27	P. S.	F	1 yr.	Acute myelitis	109.0	75.9	69.6
	Blood sugar and cerebrospinal fluid sugar in eleven nonfasting patients.						
41	V. P.	F	8 yrs.	Streptococcic meningitis	142.8	22.0	15.4
4	I. C.	M	3 yrs.	Syphilitic meningitis	96.0	74.8	77.9
8	E. K.	F	4 yrs.	Infantile cerebroparalysis	186.6	75.4	40.4
39	M. S.	M	7 yrs.	Unexplained convulsions	89.3	77.0	86.2
32	E. S.	M	4 yrs. 6 mos.	Unexplained convulsions	100.9	83.4	82.6
15	E. R.	M	7 mos.	Rickets	114.1	85.0	74.4
28	V. R.	F	4 yrs. 3 mos.	Secondary pneumonia	125.5	88.3	70.3
40	E. S.	F	10 mos.	Congenital malformation of brain	71.7	92.0	128.0
11	J. V.	M	1 yr. 6 mos.	Primary pneumonia	143.5	104.0	72.0
33	A. B.	M	3 mos.	Bacillary dysentery	175.7	134.3	76.0
38	R. H.	F	18 mos.	Acute otitis media	89.9	138.5	154.0
36	M. B.	M		Unexplained convulsions	267.4	194.3	72.6

it was between 50 and 70 mg. per hundred cubic centimeters, the average amount in the cerebrospinal fluid being 61.7 mg. In the same percentage of the cases, the sugar in the cerebrospinal fluid was from 50 to 70 per cent of that in the blood, the average being 60.3 per hundred cubic centimeters.

An examination of table 1 shows that, in a series of cases in human beings, which include poliomyelitis, encephalitis, pneumonia, infections of

the upper respiratory tract, mental retardation, unexplained convulsions, congenital malformation of the brain, infantile cerebral paralysis, sinus thrombosis and acute nephritis, the concentration of sugar in the cerebrospinal fluid in these pathologic conditions does not show sufficiently wide variation and consistency to permit diagnostic interpretation. An exception may be made in the two cases of tuberculous meningitis in which values of 40.2 and 48.1 mg. per hundred cubic centimeters were obtained, but even then 44.6 mg. was the concentration of sugar in a case of mental retardation. However, in purulent meningitis, an abnormally low concentration of sugar may be present in the cerebrospinal fluid, as was observed in one of our cases in which 22 mg. was the value obtained, and this value remained practically at that level for five hours, although glucose was given parenterally at short intervals.

We believe that the failure to realize the fact that the glucose intake affects quantitatively the content of the reducing substance in the

TABLE 2.—*Observation of Twenty-nine Patients Who Fasted Ten Hours or More*

No. of Mg. per 100 Cc.	No. of Cases	Percentage of Total No. of Cases
40-50	3	10.3
50-60	6	20.6
60-70	18	61.8
70-80	2	6.8
40-60	9	30.9
60-80	20	68.6
50-70	24	82.7

cerebrospinal fluid is responsible for the marked variability that has been obtained. That the concentration of the sugar in the cerebrospinal fluid may vary with the carbohydrate intake just as the concentration of the sugar in the blood does, is not admitted by all. Kelley [6] finds no increase in the sugar content in the cerebrospinal fluid following the injection of glucose into the blood. Becker [7] also does not note a significant increase in the reducing substance in the cerebrospinal fluid during the first hour after the oral administration of glucose. Ino,[8] however, observes an increase in the reducing substance in the cerebrospinal fluid as the content of glucose increases in the blood stream. Fremont-Smith and Daily [9] record a maximum increase of from 6 to 9 mg. per hundred cubic centimeters in the concentration of

6. Kelley, A. G.: South. M.J. **16**:407, 1923.

7. Becker, S. W.: Am. J. Syph. **11**:37, 1927.

8. Ino, I.: Acta Scholae Med. Univ. imp. Kiato **3**:No. 40, 609, 1920.

9. Fremont-Smith, F., and Daily, E.: Human Cerebro-Spinal Fluid, New York, Paul B. Hoeber, 1926, chapter 7.

sugar in the cerebrospinal fluid in four cases, during from one to one and one-half hours following oral or intravenous administration of glucose.

EXPERIMENTAL WORK ON DOGS

Experimental work was done on dogs in order to make a more complete study of the effect of the ingestion of glucose on the cerebrospinal fluid sugar. The animals were given no food for twenty-

TABLE 3.—*Summary of the Results of Estimations on the Fluid Sugar of Dogs*

Fluid	Average Time for Maximum Rise	Average Time Required to Reach Normal Level
Whole blood sugar	27 minutes	3½ hours
Plasma sugar	39 minutes	4½ hours
Cerebrospinal fluid sugar	2 hours and 36 minutes	6-7 hours

TABLE 4.—*Concentration of Reducing Substance in the Fluids Obtained from the Dogs*

	Fasting	¼ Hr.	½ Hr.	1 Hr.	2 Hrs.	3 Hrs.	4 Hrs.	5 Hrs.	6 Hrs.	7 Hrs.
Dog 1										
Blood	72.1	120.3	136.1	104.0	69.3	67.9	81.9	76.7	97.5	.....
Plasma	82.4	187.9	261.3	223.2	126.6	97.4	90.0	82.4	97.4	.....
Cerebrospinal fluid.	72.0	88.5	91.9	114.9	133.0	104.5	93.1	81.1	69.4	.....
Dog 2										
Blood	81.7	202.9	171.1	163.3	.....	134.8	133.9	114.4	106.6	105.9
Plasma	105.0	231.9	262.6	272.6	255.1	191.3	164.8	125.4	106.0	110.3
Cerebrospinal fluid.	81.2	88.5	94.8	128.4	155.2	160.8	161.8	164.8	143.8	113.8
Dog 3										
Blood	89.2	170.0	201.0	201.4	170.0	118.4	107.6	102.0	73.8	.....
Plasma	109.0	249.1	289.5	297.6	289.5	146.7	107.2	105.0	97.1	.....
Cerebrospinal fluid.	107.0	110.7	167.9	202.1	261.2	206.0	154.9	111.2	90.1	.....
Dog 4										
Blood	72.3	175.6	165.1	145.0	140.9	155.2	112.6	90.0	84.3	.....
Plasma	96.5	223.2	218.6	220.9	216.4	175.6	106.0	89.2	87.8	.....
Cerebrospinal fluid.	85.0	109.3	115.2	157.5	198.4	184.7	157.5	116.4	106.3	.....
Dog 5										
Blood	93.4	158.5	197.3	168.1	133.2	112.7	108.0	96.4	96.1	.....
Plasma	94.4	167.3	250.5	189.1	132.5	130.6	127.5	94.8	103.0	.....
Cerebrospinal fluid.	88.5	95.6	106.0	130.6	154.9	149.4	153.0	144.7	109.0	.....

four hours, and were then anesthetized with iso-amyl-ethyl (from 0.5 to 0.65 mg. of iso-amyl-ethyl in 10 per cent second normal sodium hydroxide solution per kilogram of body weight were given intraperitoneally). The cerebrospinal fluid was obtained by cisternal punctures. Estimations of sugar were made in duplicate simultaneously on whole blood, plasma and cerebrospinal fluid. The samples were drawn immediately before the intraperitoneal administration of glucose (from 0.5 to 1 Gm. per kilogram of body weight), and at intervals of fifteen minutes, one-half hour and one hour for a period of from six to seven hours. The results are given in tables 3 and 4.

Throughout this study, the Kramer and Gittleman micromethod for determination [10] of the sugar content was the procedure employed. In a comparative analysis of this technic with that of the Folin and Wu macromethod, with known sugar solutions containing from 50 to 350 mg. of glucose in a 100 cc. solution, one of us [11] found that with the Kramer and Gittleman technic, the mean error varied from 0.1 to 2.2 in mg. per hundred cubic centimeters, and from 0.4 to 1.4 in percentage, and with the latter procedure it was between 0.2 and 2.7 in mg. per hundred cubic centimeters, and between 0.1 and 3 in percentage. This indicates that the variations in the sugar content of the cerebrospinal fluid in excess of plus or minus 3 mg. per cent represented actual differences in the concentration of the sugar in the cerebrospinal fluid, and should not be attributed to error in technic.

It will be noted that following the intake of glucose the amount of sugar in the plasma and whole blood shows a marked and steep rise, reaching its maximum height in a comparatively short period of time. The increase of the sugar in the cerebrospinal fluid, on the other hand, occurs more slowly, but the maximum concentration is maintained over a longer period. The same observation can be made in the matter of the descent to the normal level. The average time for the maximum rise of the sugar in the blood is twenty-seven minutes, of the sugar in the plasma, thirty-nine minutes, and of the sugar in the cerebrospinal fluid, two hours and thirty-six minutes. The average time that these fluids require to reach a normal level in respect to their sugar content is three hours and twenty-four minutes for whole blood, four hours and twenty-four minutes for plasma and more than six to seven hours for the cerebrospinal fluid.

SUMMARY AND CONCLUSION

1. The smallest variation in concentration of the sugar in the cerebrospinal fluid was obtained in patients who had not received food for ten hours or more. It fluctuated between 40.2 and 75.9 mg. per hundred cubic centimeters, with an average content of the reducing substance of 61.7 mg.

2. Experimental work on dogs showed that following the intake of glucose, the sugar in the cerebrospinal fluid increased, but after a fairly constant and comparatively long latent period. This increase was sustained for some time, but the amount gradually returned to its previous level. The entire cycle occurred more rapidly in the blood.

3. The cencentration of sugar both in the blood and in the cerebrospinal fluid is affected by the intake of glucose.

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10. Kramer, B., and Gittleman, I. F.: Technic for Quantitative Estimation of Sugar in very Small Amounts of Blood, J. A. M. A. **30**:1171 (Oct. 3) 1923.

11. Orent, E. R.: J. Lab. & Clin. Med. **12**:No. 5, 432, 1927.

4. There is no direct parallelism between the increase or decrease of sugar in the blood and in the cerebrospinal fluid. However, during the postabsorptive period, there is a more definite correlation between the concentration of sugar in the blood and in the cerebrospinal fluid.

5. During the absorptive period, in the specimens of fluid obtained simultaneously, the concentration of sugar in the whole blood and in plasma may be equal to, greater than or less than that of the cerebrospinal fluid. In the postabsorptive period, the sugar content of cerebrospinal fluid is always less than that of the blood or blood plasma.

6. To place any diagnostic significance on the sugar content of the cerebrospinal fluid, it must be determined on fluid that has been obtained from a fasting person, preferably after a fast of ten hours or more.

EPILEPSY IN CHILDREN

RELATIONSHIP OF VARIATIONS IN THE DEGREE OF KETONURIA TO OCCURRENCE OF CONVULSIONS IN EPILEPTIC CHILDREN ON KETOGENIC DIETS *

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It has been definitely established by the work of Wilder,[1] Peterman,[2] Talbot, Metcalf and Moriarty [3] and others that children suffering from idiopathic epilepsy are greatly benefited by a diet high in fat and sufficiently low in carbohydrate and protein to produce ketosis. The effects of the ketogenic diet are similar to those of fasting, as regards changes in the patient's blood [4] and in his clinical condition. Just how such forms of dietary regulation effect the striking improvement often seen in cases of genuine epilepsy is not entirely clear. Wilder attributes the change to the anesthetic action of the acetone bodies, particularly the aceto-acetic acid. Other observers suggest that it is due to the mild acidosis produced. The latter opinion is based on the observations of Jarloev [5] and Bigwood [6] that the convulsive seizures are frequently preceded by a slight shifting of the blood plasma reaction toward alkalinity. Whatever explanation may finally prove correct, most persons who have had

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* From the Department of Pediatrics, University of Rochester, and the Pediatric Service of the Strong Memorial Hospital.

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1. Wilder, R. M.: The Effects of Ketonuria on the Course of Epilepsy, Mayo Clinic Bull. **2**:307, 1921.

2. Peterman, M. G.: The Ketogenic Diet in the Treatment of Epilepsy, Am. J. Dis. Child. **28**:28 (July) 1924; The Ketogenic Diet in Cases of Epilepsy, J. A. M. A. **84**:1979 (June 27) 1925.

3. Talbot, F. B.; Metcalf, K., and Moriarty, M.: The Ketogenic Diet in the Treatment of Idiopathic Epilepsy, Tr. Am. Pediat. Soc. **38**:30, 1926; and Am. J. Dis. Child. **32**:316 (Aug.) 1926; Epilepsy: Chemical Investigations of Rational Treatment by Production of Ketosis, Am. J. Dis. Child. **33**:218 (Feb.) 1927.

4. Talbot, Metcalf and Moriarty (footnote 3, second part).

5. Jarloev, E.: Sur l'equilibre acido-basique du sang humain, Etudié dans ses rapports avec diverses affections, Compt. rend. Soc. de biol. **84**:156, 1921.

6. Bigwood, E. J.: Disturbance of the Acid-Base Equilibrium of the Blood in Epilepsy, Compt. rend. Soc. de biol. **89**:818, 1923.

extensive experience with this form of treatment now agree that there is a direct relationship between the degree of improvement and the intensity of the ketosis produced.

The observation that certain epileptic children who were definitely benefited by a ketogenic diet continued to have occasional morning convulsions in spite of it suggested to us the need of information regarding variations in the degree of ketosis during the day under such conditions. The investigation reported here was undertaken to furnish such data.

METHOD

The general plan of procedure was that of determining variations in the rate of excretion of the acetone bodies in the urine and their concentration in the blood throughout the day. Because the first epileptic subject observed to have morning convulsions while on the ketogenic diet was too young to cooperate satisfactorily in the collection of samples, normal children between the ages of 11 and 13 years were selected for the initial study. Later, two epileptic patients of this age became available also. All the subjects were kept in bed on approximately maintenance diets, so regulated that varying degrees of ketosis would result. The total rations for the day were divided into either three or four meals of equal value as regards their content of protein, fat and carbohydrate. These were given at five hour intervals during the day, the first at 7 a. m. In one case the diet was preceded by a ninety hour fast. In the others the change from the ordinary, relatively high carbohydrate diet to the high fat diet was abrupt.

After ketosis was shown to be established by qualitative tests for acetone and aceto-acetic acid in the urine, samples were collected in two and one-half hour or five hour periods throughout the day and night. The volume of output of the urine was controlled in part by having the subject drink 100 cc. of water at the beginning of each collection period. The acetone bodies were determined by the colorimetric method of Behre and Benedict,[7] and all values are expressed in terms of acetone. When determinations could not be made immediately, the specimens were placed in the icebox in tightly stoppered bottles containing copper sulphate as a preservative. Samples of blood were taken at different periods of the day for estimation of the acetone bodies. Incidentally, sugar determinations were made at the same time on many of the samples because of the observation by Josephs[8] that hypoglycemia may occasionally be the cause of morning convulsions in nonepileptic children.

REPORT OF CASES

CASE 1.—*History.*—D. S., a girl, aged 13, was admitted, March 21, 1927, because of severe convulsions which had occurred for the first time one year previously. The patient had always been well before the onset of the convulsions, which were not preceded by febrile disease. Birth and the postnatal history were normal. The patient had gained weight at an inordinate rate during

7. Behre, J. A., and Benedict, S. R.: A Colorimetric Method for the Determination of Acetone Bodies in Blood and Urine, J. Biol. Chem. **70**:487, 1926.

8. Josephs, H.: Fasting as a Cause of Convulsions, Am. J. Dis. Child. **31**:169 (Feb.) 1926.

the previous six months, following the onset of the the menses. The attacks had become more frequent, averaging about two weekly at the time of admission. They were usually severe, and often were followed by excessive muscular activity. The attack observed on admission, said by the mother to be typical, was generalized in character, with tonic and clonic phases. It was preceded by aura, accompanied by a complete loss of consciousness, falling over, frothing at the mouth, dilatation of the pupils, biting of the tongue and loss of control of the bladder and was followed by drowsiness and mental dulness.

Physical Examination.—This examination did not reveal any abnormalities except obesity and a slight diffuse enlargement of the thyroid gland. The secondary sex characters were well developed. Neurologic examination, including study of the visual fields, did not reveal any abnormalities. Definite mental retardation was not observed. A roentgenogram of the skull showed that the sella turcica was normal. The blood Wassermann and tuberculin reactions were negative. The basal metabolic rate was normal. The diagnosis was: (1) probably idiopathic epilepsy, (2) obesity.

Course.—After three days' fast, the patient was placed on a ketogenic diet for five days, and then on high carbohydrate diet for one week. Convulsions did not occur during this period, except for possible petit mal on the third day of the carbohydrate diet. Menstruation occurred during the period of observation. The girl was discharged from the hospital on a 1,000 calory obesity diet which contained approximately 60 Gm. each of protein and carbohydrate. Two months after discharge, the attacks had not recurred.

CASE 2.—*History.*—M. P., an Italian girl, aged 12, was admitted to the hospital, Jan. 25, 1927, because of convulsions at frequent intervals over a period of five years. The seizures were said to be increasing in frequency and severity. The first appearance of the convulsions was said to be unrelated to any injury or acute illness. Birth and the early development, apparently, were entirely normal. The convulsions were always generalized, with tonic and clonic phases. They were preceded by aurae, such as "queer sensations in stomach." During the attacks, consciousness was always lost completely for a few minutes; the patient would fall, often injuring herself; loss of control of the bladder and frothing at the mouth were frequently observed. The seizures were usually followed by sleep and mental dulness. The patient was backward in school.

Physical Examination.—The girl was well developed and well nourished. She weighed 36 Kg. The face was dull in expression, showing many skin marks of acne vulgaris. The teeth were carious. The thyroid isthmus was moderately thickened. Otherwise, the observations were entirely negative. The tuberculin and blood Wassermann reactions were negative. The patient was rated by mental tests as being in "high grade defective group." Neurologic examination was negative. The diagnosis was idiopathic epilepsy.

Course.—During the first twenty-four hours after admission, without treatment, the patient had five fairly severe convulsive seizures. Opiates partly controlled the seizures on the second day. A diet containing a limited amount of carbohydrates and as much fat as the patient would take was prescribed. This resulted in the production of a marked degree of ketosis at the end of three days, accompanied by a cessation of the convulsions and improvement in the patient's attitude. After six days of this regimen, a diet containing 44 Gm. each of protein and carbohydrate and 252 Gm. of fat was prescribed. Two days later, coincident with a decrease in the degree of ketosis, convulsions

began, occurring every morning for one week, until the diet was replaced by one which was more strongly ketogenic. After thirty-six hours on the latter diet, the convulsions ceased, recurring only when the diet was broken on an occasion one week later and again when insulin and a large meal of carbohydrate were administered.

EXPERIMENTAL RESULTS

The present report deals chiefly with observations made on the urinary acetone bodies. Data bearing on the blood ketones will be presented in a future communication. However, it may be said here that the concentration of the acetone bodies in the blood has been found to run parallel to that in the urine. An example of this is shown incidentally in table 6. The blood sugar values have remained well within the normal limits in both nonepileptic and epileptic subjects.

It is obvious from inspection of the accompanying tables and charts that the rate of excretion of acetone bodies fluctuates markedly during the day, under the conditions outlined. When all the meals of the diet are completely consumed, the variations tend to be uniform from day to day. The lowest rate of excretion occurs, characteristically, during the morning hours, from 3 to 9: 30 a. m., and the maximum rate during the late afternoon. After the high peak has been reached, there is a gradual decrease to the minimum level next morning, unless an additional meal is given, in which event a secondary rise usually follows. In a separate study of the respiratory metabolism in normal and epileptic children on ketogenic diets, being made jointly with Dr. R. S. Lyman,[9] it was observed that the value of the respiratory quotient of subject M. B. (table 1) was roughly proportional inversely to the rate of excretion of acetone bodies. Both the total and the nonprotein respiratory quotients were approximately 0.08 higher before breakfast in the morning, when the ketone excretion was low, than at 3: 15 p. m., when it was near the maximum rate for the day.

Chart 1 shows the typical variations, even during the period of increasing ketosis in the first days of the diet, while chart 2 shows the tendency to regularity in these variations from day to day, after the degree of ketosis has reached its high level for a given diet. The latter shows, also, the evening drop in the excretion rate, with a subsequent rise after the fourth meal. However, these minor variations are usually seen in the two and one-half hour periods only, frequently being too small to be in evidence when the data are plotted for five hour periods alone.

Table 1, from which charts 1 and 2 were taken, shows, in addition, the relationship between volume of urine and excretion of acetone bodies. While the concentration of ketones in the urine is lowest in the morning and highest in the afternoon, it is apparent that the variations in their output during the day is dependent to a slight degree only on the volume

9. Lyman, R. S.: Unpublished work.

TABLE 1.—*Variations in Rate of Excretion of Acetone Bodies at Different Times of Day by Normal Children on Ketogenic Diets—Two and One-Half Hour Periods—Four Meals*

Date, 1927	Period of Day	Volume of Urine, Cc.	Total Acetone Bodies for Period, Mg.	Total Acetone Bodies per 100 Cc., Mg.	Miscellaneous
2/26	7:00- 9:30 a.m.	182	6.1	3.3	M. B., a girl, aged 12; weight, 32 Kg.
	9:30-12:00 m.	154	14.0	9.0	Diet: fats, 200 Gm.; protein, 32
	12:00- 2:30 p.m.	131	151.1	115.3	Gm.; carbohydrate, 28 Gm.
	2:30- 5:00 p.m.	194	384.7	193.1	Meals: 7 a.m., 12 m., 5 p.m., 10
	5:00- 7:30 p.m.	338	231.2	68.4	p.m.
	7:30-10:00 p.m.	139	84.4	60.7	All food eaten
2/27	10:00-12:30 a.m.	94	150.0	159.4	
	12:30- 3:00 a.m.	152	86.3	56.8	
	3:00- 5:30 a.m.	106	75.7	71.4	
	5:30- 8:00 a.m.	196	35.6	18.1	
	8:00- 9:30 a.m.	183	37.3	20.3	
	9:30-12:00 m.	287	97.3	33.9	
	12:00- 2:30 p.m.	395	225.7	57.1	
	2:30- 5:00 p.m.	156	539.5	345.8	
	5:00- 7:30 p.m.	336	548.5	163.2	
	7:30-10:00 p.m.	84	389.5	463.7	
2/28	10:00-12:30 a.m.	100	389.9	389.9	
	12:30- 3:00 a.m.	230	246.4	107.1	
	3:00- 5:30 a.m.	237	105.6	44.5	
	5:30- 8:00 a.m.	58	47.3	29.9	
	8:00- 9:30 a.m.	113	52.4	46.3	
	9:30-12:00 m.	238	124.1	52.1	
	12:00- 2:30 p.m.	119	214.7	180.4	
	2:30- 5:00 p.m.	249	956.1	383.9	
	5:00- 7:30 p.m.	82	263.0	320.7	
	7:30-10:00 p.m.	110	388.2	352.7	
3/ 1	10:00-12:30 a.m.	...	.....	.....	Specimen lost
	12;30- 3:00 a.m.	190	243.8	128.3	
	3:00- 5:30 a.m.	115	98.5	85.6	
	5:30- 8:00 a.m.	250	85.2	34.1	
1/22	7:00- 9:30 a.m.	68	7.3	10.7	G. B., a girl, aged 11
	9:30-12.00 m.	68	24.9	36.6	Diet: fat, 180 Gm.; protein, 30
	12:00- 2:30 p.m.	62	104.2	168.0	Gm.; carbohydrate, 30 Gm.
	2:30- 5:00 p.m.	310	279.3	90.1	In four equal meals as in fore-
	5:00- 7:30 p.m.	126	236.6	187.7	going case
	7:30-10:00 p.m.	55	67.0	121.8	All food eaten
1/23	10:00-12:30 a.m.	48	112.5	234.2	
	12:30- 3:00 a.m.	124	170.1	136.6	
	3:00- 5:30 a.m.	230	18.4	8.0	
	5:30- 8:00 a.m.	256	18.5	7.2	
1/24	.....	...	.....	.....	Diet continued
1/25	7:00- 9:30 a.m.	360	38.3	10.6	
	9:30-12:00 m.	65	52.2	80.3	
	12:00- 2:30 p.m.	152	108.8	71.5	All food eaten
	2:30- 5:00 p.m.	155	268.0	172.8	
	5:00- 7:30 p.m.	110	201.2	182.7	
	7:30-10:00 p.m.	160	126.3	78.9	
1/26	10:00-12:30 a.m.	60	53.0	88.3	
	12:30- 3:00 a.m.	365	148.9	40.8	
	3:00- 5:30 a.m.	275	39.7	14.4	
	5:30- 8:00 a.m.	65	2.2	3.4	

of urine. This indicates the absence of any diuretic effect of the acetone bodies comparable to that of urea, glucose or the inorganic salts, when such are present in the body in excessive amounts.

The figures in table 2 show the effect of preliminary fasting on variations in the output of acetone bodies by a subject on the ketogenic diet. It is apparent that during the ninety hour fasting period and during the first forty-eight hours of the ketogenic diet given at the termination of

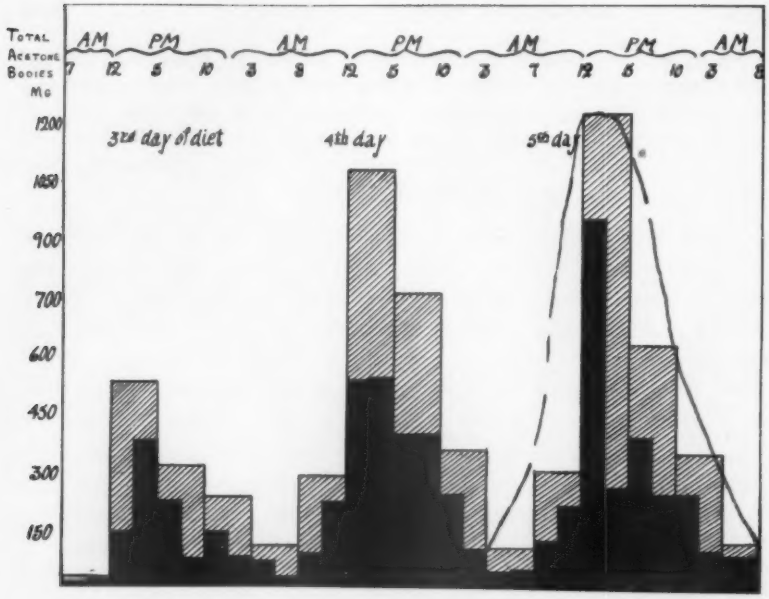

Chart 1.—Variations in the rate of excretion of acetone bodies during the third, fourth and fifth days of ketogenic diet in M. B., a normal girl, aged 12, weighing 32 Kg. Diet: protein, 32 Gm.; carbohydrate, 28 Gm.; fat, 200 Gm. Absolute quantities of total acetone bodies for two and one-half hour periods are represented by the smaller columns in black. The same data expressed in five hour periods are shown in the columns faced with oblique lines.

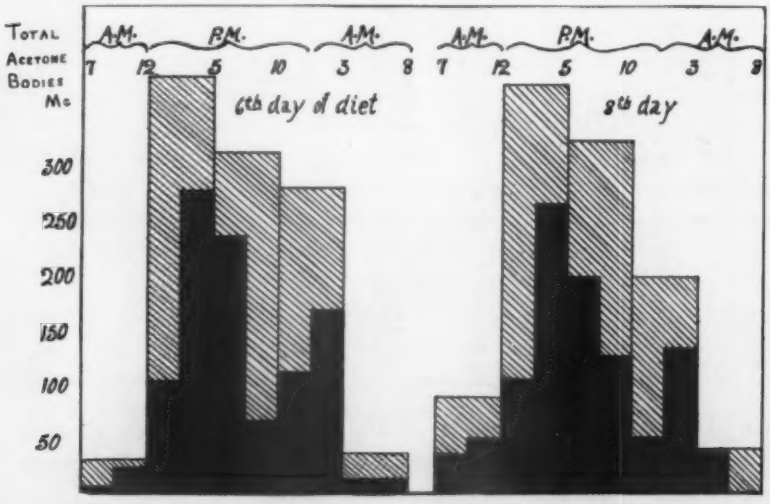

Chart 2.—Typical variations in the excretion of acetone bodies during the day when four ketogenic meals are eaten. The more or less characteristic evening decline followed by a secondary rise after the fourth meal, as shown in black shading, is usually observed in the shorter periods only. Such minor variations are obliterated when the five hour periods alone are charted. The patient was G. B., a normal girl, aged 11, weighing 30 Kg. Diet: protein, 30 Gm.; carbohydrate, 30 Gm.; fat, 180 Gm.

the fast, the curve of excretion did not tend definitely to follow the curve found in the previous cases. On the third day of the diet, however, the characteristic low rates for morning and the high rates for afternoon were found. From this time on, the variations were almost identical with those observed in subjects who changed abruptly from a high carbo-

TABLE 2.—*Effect of Ninety-Hour Preliminary Fast on Variations in Rate of Excretion of Acetone Bodies by Obese Child on Ketogenic Diet—Five-Hour Collection Periods*

Date, 1927	Period of Day	Volume of Urine, Cc.	Total Acetone Bodies for Period, Mg.	Total Acetone Bodies per 100 Cc., Mg.	Miscellaneous
3/22	7:00-12:00 m.	202	8	4	D. S., obese, mildly epileptic, aged 13, weight 62 Kg.; last food at 5 p.m. 3/21/27; water given as required
	12:00- 5:00 p.m.	635	48	8	
	5:00-10:00 p.m.	297	48	16	
3/23	10:00- 3:00 a.m.	95	43	45	
	3:00- 8:00 a.m.	80	137	165	
3/23	8:00-12:00 m.*	101	569	563	
	12:00- 5:00 p.m.	357	1,123	314	
	5:00-10:00 p.m.	470	1,410	300	
3/24	10:00- 3:00 a.m.	145	1,564	1,072	
	3:00- 7:00 a.m.*	213	2,130	1,000	
3/24	7:00-12:00 m.	315	3,000	952	
	12:00- 5:00 p.m.	329	2,371	720	
	5:00-10:00 p.m.	322	2,064	641	
3/25	10:00- 3:00 a.m.	206	2,060	1,000	
	3:00- 8:00 a.m.	239	1,992	833	
3/25	8:00-12:00 m.*	225	3,214	1,428	Diet: fat, 200 Gm.; protein, 32 Gm.; carbohydrate, 28 Gm. First meal at 8 a.m. 3/26/27. Meals at 7 a.m., 12 m. and 5 p.m.
	12:00- 5:00 p.m.	215	1,599	744	
	5:00-10:00 p.m.	318	1,856	583	
3/26	10:00- 3:00 a.m.	170	1,214	714	
	3:00- 7:00 a.m.*	135	966	715	
3/26	7:00-12:00 m.	180	729	405	
	12:00- 5:00 p.m.	200	1,600	800	
	5:00-10:00 p.m.	250	1,049	419	All food eaten
3/27	10:00- 3:00 a.m.	240	1,299	542	
	3:00- 7:00 a.m.*	340	1,312	386	
3/27	7:00-12:00 m.	240	320	133	
	12:00- 5:00 p.m.	250	1,577	631	
	5:00-10:00 p.m.	405	1,002	247	
3/28	10:00- 3:00 a.m.	230	1,022	444	All food eaten
	3:00- 8:00 a.m.	130	254	195	
3/28	8:00-12:00 m.*	208	467	224	
	12:00- 5:00 p.m.	262	1,474	563	
	5:00-10:00 p.m.	400	1,745	436	All food eaten
3/29	10:00- 3:00 a.m.	240	457	190	
	3:00- 7:00 a.m.*	170	220	130	
3/29	7:00-12:00 m.	212	423	199	
	12:00- 5:00 p.m.	435	1,726	397	
	5:00-10:00 p.m.	800	2,039	255	
3/30	10:00- 3:00 a.m.	415	467	112	All food eaten
	3:00- 8:00 a.m.	260	272	104	

* Values obtained were multiplied by 5/4 to approximate five hour values.

hydrate to a high fat diet, except for the fact that the relative difference between the rates of excretion in the morning and in the afternoon was much smaller, because of the preliminary fast.

Since the respiratory quotient (0.708) at the end of the fasting period indicated a fairly marked depletion of the readily available tissue glycogen, it is interesting to inquire into the cause for the diminution in intensity of ketonuria during the morning periods after the first two days

TABLE 3.—*Urinary Acetone Bodies of Children on High Fat, High Carbohydrate and Borderline Diets—Five-Hour Periods—Three Equal Meals*

Date, 1927	Period of Day	Volume of Urine, Cc.	Total Acetone Bodies for Period, Mg.	Total Acetone Bodies per 100 Cc., Mg.	Miscellaneous
3/30	7:00-12:00 m.	350	700	200	D. S., obese; weight, 62 Kg.
	12:00- 5:00 p.m.	605	1,583	261	Diet: protein, 32 Gm.; fat, 200
	5:00-10:00 p.m.	430	860	200	Gm.; carbohydrate, 28 Gm.
3/31	10:00- 3:00 a.m.	200	368	180	K/A.K.* (Woodyatt) 3:1
	3:00- 8:00 a.m.	160	155	96	
3/31	8:00-12:00 m.†	170	418	245	Fast preceding ketogenic diet
	12:00- 5:00 p.m.	250	952	381	
	5:00-10:00 p.m.	490	1,314	268	
4/1	10:00- 3:00 a.m.	170	492	289	
	3:00- 8:00 a.m.	150	326	217	
4/1	8:00-12:00 m.†	670	83.7	12.5	Diet: protein, 32 Gm.; fat, 36
	12:00- 5:00 p.m.	550	19.4	3.5	Gm.; carbohydrate, 400 Gm.
	5:00-10:00 p.m.	400	15.3	3.8	K/A.K.* 1:9
4/2	10:00- 3:00 a.m.	100	4.1	4.1	
	3:00- 8:00 a.m.	100	4.1	4.1	
4/3	8:00-12:00 m.†	150	6.5	4.3	
	12:00- 5:00 p.m.	190	9.1	4.7	
	5:00-10:00 p.m.	410	16.4	4.0	
4/4	10:00- 3:00 a.m.	90	4.3	4.8	
	3:00- 8:00 a.m.	120	5.3	4.4	
4/4	8:00-12:00 m.†	430	21.7	5.0	
	12:00- 5:00 p.m.	430	17.6	4.1	
	5:00-10:00 p.m.	570	22.7	3.9	
4/5	10:00- 3:00 a.m.	160	6.7	4.2	
	3:00- 8:00 a.m.	200	7.4	3.6	
3/26	8:00-12:00 m.†	50	21.5	43.0	R. M., aged 3½; weight, 17 Kg.
	12:00- 5:00 p.m.	340	112.9	33.2	Borderline diet: protein, 12 Gm.;
	5:00-10:00 p.m.	140	96.5	68.9	fat, 60 Gm.; carbohydrate, 18
3/27	10:00- 3:00 a.m.	130	19.5	15.0	Gm.
	3:00- 8:00 a.m.	69	3.5	5.0	K/A.K.* 1.6:1
3/27	8:00-12:00 m.†	250	96.1	38.4	
	12:00- 5:00 p.m.	341	183.9	53.9	
	5:00-10:00 p.m.	332	88.5	26.6	
3/28	10:00- 3:00 a.m.	100	18.5	18.5	
	3:00- 8:00 a.m.	60	11.0	18.3	
3/28	8:00-12:00 m.†	240	45.3	18.7	Diet: protein, 12 Gm.; fat, 60 Gm.;
	12:00- 5:00 p.m.	250	72.1	28.8	carbohydrate, 38 Gm.
	5:00-10:00 p.m.	350	14.8	4.2	K/A.K.* 1.16:1
3/29	10:00- 3:00 a.m.	100	6.7	6.7	
	3:00- 8:00 a.m.	90	5.1	5.6	
3/29	8:00-12:00 m.†	340	16.3	4.8	
	12:00- 5:00 p.m.	240	14.3	5.9	
	5:00-10:00 p.m.	580	25.1	4.3	
3/30	10:00- 3:00 a.m.	90	5.5	6.0	
	3:00- 8:00 a.m.	60	9.3	15.5	

* $\frac{\text{Gm. Fatty Acid}}{\text{Gm. Glucose}}$

† Values found for period were multiplied by 5/4 to approximate five hour values.

of this diet. It seems almost incredible that glycogen should be stored by an obese subject from a rather strongly ketogenic diet, the total caloric value of which was slightly below the maintenance level. Under other circumstances, acidosis per se is known to exert a glycogenolytic effect.[10] After the first two days of the ketogenic diet, during which the daily output of acetone was being reduced to a new level two thirds below that observed

10. Lusk, G.: Science of Nutrition, ed. 3, Philadelphia, W. B. Saunders Company, 1917, p. 447.

for the last day of the fast, small amounts of glycogen apparently were stored in the tissues during the absorptive period of the day only to be utilized the next morning in the process of ketolysis. Additional support for this assumption is given by the fact that the respiratory quotient was always higher in the postabsorptive period than during the afternoon. Incidentally, it is of interest, however, that the difference between the morning and afternoon respiratory quotients, namely, about 0.04, was only one half that observed in the previous cases, in which carbohydrate feeding immediately preceded the use of the ketogenic diet. This indicates the presence of a much smaller store of glycogen in the tissues of the person subjected to the preliminary fast.

The data in table 3 show the comparative effects of different diets on variations in the rate of excretion of acetone bodies. It is evident that there is no tendency for an increase in the afternoon or a decrease in the morning in the rate of excretion when a high carbohydrate diet is taken. There is a slight tendency for a rise in the afternoon, however, when the person is on the so-called "borderline diet." This observation confirms that of Hubbard and Wright,[11] who made an extensive study of the excretion of acetone bodies in adults on borderline diets, such as are prescribed for patients with diabetes mellitus or chronic arthritis.

In tables 4 and 5 and in chart 3 are presented the results of observations made in the case of a 12 year old girl, M. P., suffering from severe idiopathic epilepsy. Chart 3, taken from table 4, shows graphically the time relationship between the occurrence of convulsions and the minimum degree of ketonuria.

The period of observation, denoted by the dates in table 4, was preceded by an interval of one week, during which ketosis was sufficiently marked to prevent seizures entirely. It is significant that the gradual diminution in the degree of ketonuria observed in this instance is attributable apparently to the low magniture of the ratio

$$\frac{\text{Ketogenic molecules actually metabolized}}{\text{Antiketogenic molecules in portion of diet utilized}}$$

rather than to any fault in the ratio of ketogenic to antiketogenic materials fed, or to a break in the diet. The intensity of the ketosis depends, of course, on the relative proportions of fatty acids and glucose which actually undergo combustion and not on the proportions in which they may occur in the diet. At the border line of ketosis, as found by Shaffer,[12] Woodyatt [13] and others, each molecule of glucose is ketolytic

11. Hubbard, R. S., and Wright, F. R.: Variations in the Rate of Excretion of the Acetone Bodies During the Day, J. Biol. Chem. **61**:377, 1924.

12. Shaffer, P. A.: Antiketogenesis; Its Mechanism and Significance, Medicine **2**:375, 1923.

13. Woodyatt, R. T.: Objects and Method of Diet Adjustment in Diabetes, Arch. Int. Med. **28**:125 (Aug.) 1921.

TABLE 4.—*Urinary Acetone Bodies of Epileptic Subject on Ketogenic Diet Showing Relationship Between Occurrence of Convulsive Seizures and Changes in Degree of Ketonuria at Different Periods of the Day—Diminishing Ketosis Due to Overestimating Food Requirements*

Date, 1927	Period of Day	Volume of Urine, Cc.	Total Acetone Bodies for Period, Mg.	Total Acetone Bodies for 100 Cc., Mg.	Convulsive Seizures	Remarks
2/3	7:00- 9:30 a.m.	67	5.9	8.8	At 7 a.m.	M. P., aged 12; weight,
	9:30-12:00 m.	72	21.3	30	mild	38 Kg. Diet: protein,
	12:00- 2:30 p.m.	96	102.8	107		44 Gm.; carbohydrate,
	2:30- 5:00 p.m.	104	114.7	110		44 Gm.; fat, 252 Gm.
	5:00- 7:30 p.m.	178	34.2	19		Taken well
	7:30-10:00 p.m.	434	141.3	32.5		
2/4	10:00-12:30 a.m.	186	30.7	16		
	12:30- 3:00 a.m.	425	262.6	61		
	3:00- 5:30 a.m.	520	39.0	7.5		
	5:30- 8:00 a.m.	228	15.2	6.6	At 7:20 a.m. severe	Blood sugar, 90 mg.
2/5	7:00- 9:30 a.m.	47	16.0	34	At 5:30 a.m.	
	9:30-12:00 m.	57	27.5	48	moderately	
	12:00- 2:30 p.m.	196	73.5	38	severe	Diet taken well
	2:30- 5:00 p.m.	120	148.0	123		
	5:00- 7:30 p.m.	153	116.6	76		
	7:30-10:00 p.m.	70	64.2	92		
2/6	10:00-12:30 a.m.	143	129.2	90		
	12:30- 3:00 a.m.	252	21.9	9		
	3:00- 5:30 a.m.	408	11.0	3	At 3:45 a.m.	Blood sugar, 90 mg. at
	5:30- 8:00 a.m.	314	5.1	2	severe	7:45
2/7	7:00- 9:30 a.m.	58	10.6	18	At 5:45 a.m.	
	9:30-12:00 m.	63	26.2	41	mild	
	12:00- 2:30 p.m.	65	80.2	123	.....	Diet taken well
	2:30- 5:00 p.m.	60	124.0	206		
	5:00- 7:30 p.m.	60	41.8	69		
	7:30-10:00 p.m.	381	116.0	30		
2/8	10:00-12:30 a.m.	155	77.5	50		
	12:30- 3:00 a.m.	645	74.4	11		
	3:00- 5:30 a.m.	250	18.2	7	At 8:43 a.m.	
	5:30- 8:00 a.m.	446	8.0	2	severe	
					At 4:30 a.m.	Blood sugar, 80 mg.
2/9	7:00- 9:30 a.m.	200	65.3	32	severe	
	9:30-12:00 m.	60	23.2	39		
	12:00- 2:30 p.m.	70	19.0	27	At 1:05 p.m.	Very mild
	2:30- 5:00 p.m.	155	18.8	12.1	At 3:00 p.m.	Mild; blood sugar, 74
	5:00- 7:30 p.m.	320	34.5	11		mg.; portion of diet
	7:30-10:00 p.m.	352	50.7	14		refused
2/10	10:00-12:30 a.m.	400	55.0	13.7	At 11:37 p.m.	Mild
	12:30- 3:00 a.m.	328	49.2	15		
	3:00- 5:30 a.m.	220	16.8	8	At 3:10 a.m.	Severe
	5:30- 8:00 a.m.	80	1.7	2	At 6:10 a.m.	Very severe
2/11	.....	...	.....	.....	Six during day	Low grade ketosis

for one molecule of aceto-acetic acid; that is, the amount derived from each molecule of fatty acid which does not undergo complete oxidation, $\frac{\text{Gm. F. A.}}{\text{Gm. G.}} = \frac{1.5}{1}$. According to Shaffer, when ketones are present in great excess, one molecule of glucose is sufficient for the complete combustion of two ketogenic molecules. Clinical confirmation of the latter

relationship is found in the reports of Wilder and Winter [14] and of Palmer and Ladd.[15]

The diet of this patient, which was started the day before the period under discussion, consisted of 44 Gm. each of protein and carbohydrate and 252 Gm. of fat, with a total caloric value of 2,704 and a fatty acid to glucose ratio of 2.6:1. This was taken well for the first five days. Her basal energy requirement was estimated, according to the Benedict and Talbot [16] standard, to be about 1,300 calories. If the liberal allowance of 25 per cent for specific dynamic action and muscular activity (bed) is added to this, the total energy metabolism per day was approximately 1,625 calories. Since it may be safely assumed that the

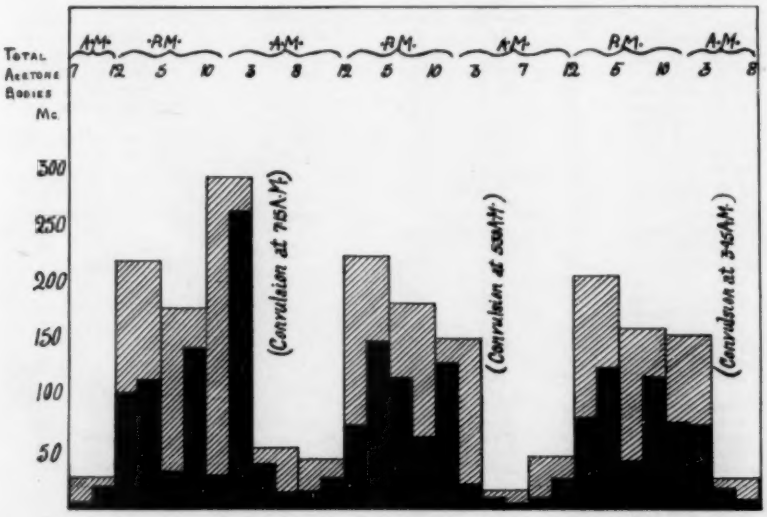

Chart 3.—Time relationship between occurrence of convulsions and minimum degree of ketosis as shown over a period of three days. Gradually diminishing ketosis due to excessive caloric value of diet in M. P., an epileptic girl, aged 12, weighing 36 Kg. Diet (started on previous day): protein, 44 Gm.; carbohydrate, 44 Gm.; fat, 252 Gm.

relatively small quantities of protein and carbohydrate allowed were completely metabolized, the estimated difference of 1,079 calories between the energy value of the diet and that of the metabolism must be accounted

14. Wilder, R. M., and Winter, M.D.: The Threshold of Ketogenesis, J. Biol. Chem. **52**:393, 1922.

15. Palmer, W. W., and Ladd, W. S.: The Use of Fat in Diabetes Mellitus and the Carbohydrate Fat Ratio, Am. J. M. Sc. **166**:157, 1923.

16. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Washington, D. C., Carnegie Institution of Washington, 1921, Publication no. 302

for as stored or unabsorbed fat to the amount of 116 Gm. The materials actually metabolized, therefore, consisted approximately of 44 Gm. of protein, 44 Gm. of carbohydrate and 136 Gm. of fat, with a fatty acid to glucose ratio of 1.7 : 1, which is consistent with the diminishing degree of ketosis observed.

TABLE 5.—*Urinary Acetone Bodies of Epileptic Subject on Ketogenic Diet—Relationship Between Occurrence of Convulsive Seizures and Change in Degree of Ketonuria at Different Times of Day—Satisfactory Diet*

Date, 1927	Period of Day	Volume of Urine, Cc.	Total Acetone Bodies for Period, Mg.	Total Acetone Bodies for 100 Cc., Mg.	Convulsive Seizures	Remarks
2/12	7:00- 9:30 a.m.	127	75.7	59.6	At 7:15 a.m.	Blood sugar, 90 mg.
	9:30-12:00 m.	66	152.7	231.4	mild	Diet: protein, 32 Gm.; fat, 200 Gm.; carbohydrate, 28 Gm.
	12:00- 2:30 p.m.	64	234.1	365.7		
	2:30- 5:00 p.m.	67	415.3	619.8		
	5:00- 7:30 p.m.	59	311.6	528.1		
	7:30-10:00 p.m.	123	290.0	230.9	At 8:50 p.m.	Nurse not certain that
	10:00-12:30 a.m.	71	304.0	428.1	petit mal?	this was seizure
2/13	12:30- 3:00 a.m.	105	219.9	209.4		
	3:00- 5:30 a.m.	297	46.1	22.2		
	5:30- 8:00 a.m.	161	103.8	64.4	At 7:25 a.m.	Mild
					none	
2/14	7:00- 9:30 a.m.	41	56.0	136.6		
	9:30-12:00 m.	61	122.0	200.0		
	12:00- 2:30 p.m.	41	66.4	162.0	.....	All food eaten
	2:30- 5:00 p.m.	47	146.8	312.3	None	
	5:00- 7:30 p.m.	50	68.2	134.4		
	7:30-10:00 p.m.	49	28.0	57.1		
	10:00-12:30 a.m.	69	80.0	115.9		
2/15	12:30- 3:00 a.m.	123	34.6	28.1		
	3:00- 5:30 a.m.	107	50.0	46.7		
	5:30- 8:00 a.m.	39	18.8	48.2		
					None	
2/19	7:00- 9:30 a.m.	146	31.5	21.6		
	9:30-12:00 m.	376	130.7	34.7		
	12:00- 2:30 p.m.	208	275.3	132.3	.....	All food eaten
	2:30- 5:00 p.m.	176	295.8	168.0		
	5:00- 7:30 p.m.	166	264.4	159.2	None	
	7:30-10:00 p.m.	412	205.1	49.7		
	10:00-12:30 a.m.	56	176.8	315.7		
2/20	12:30- 3:00 a.m.	218	133.4	61.2		
	3:00- 5:30 a.m.	142	15.1	10.6		
	5:30- 8:00 a.m.	508	89.1	17.5		
					None	
2/21	7:00- 9:30 a.m.	82	11.1	13.5		
	9:30-12:00 m.	161	61.8	38.3		
	12:00- 2:30 p.m.	148	62.5	42.2		
	2:30- 5:00 p.m.	64	70.2	109.7		
	5:00- 7:30 p.m.	28	8.4	30.0	At 7:47 p.m.	Broke diet by eating
	7:30-10:00 p.m.	45	89.2	198.2	mild	orange brought by visitor
	10:00-12:30 a.m.	246	67.9	26.7		
2/22	12:30- 3:00 a.m.	355	19.9	5.6	At 2:30 a.m.	Mild
	3:00- 5:30 a.m.	346	16.6	4.7		
	5:30- 8:00 a.m.	135	28.9	21.5		

The period of observation represented in table 5 followed that just described, with two days intervening during which the degree of ketosis reached an extremely low level. On the previous day, February 11, the patient had six severe convulsions. At noon on the same day, however, a new diet containing 32 Gm. of protein, 28 Gm. of carbohydrate and 200 Gm. of fat, with a fatty acid to glucose ratio of 2.9 : 1, was begun. This was taken well during the following ten days, and the degree of

ketosis was much more marked than on the preceding diet, which contained 52 Gm. more of fat. When the same calculations are applied to these data as to the preceding, it is seen that approximately 148 Gm. of the fat was metabolized along with the protein and carbohydrate, giving a fatty acid to glucose ratio of 2.4:1, as against 1.7:1 in the first example.

Another point of interest illustrated here is that the beneficial effect of ketosis is apparently less marked immediately after a series of convulsions. This delay in response was evident during the first twenty-four hours of the period. During this time there were two mild seizures in the morning and possibly one slight attack of petit mal in the evening,

TABLE 6.—*Relationship of Sudden Reduction of Ketosis to Recurrence of Convulsive Seizures in Epileptic Child on Ketogenic Diet—M.P., Feb. 25, 1927*

Time of Day	Total Acetone Bodies of Urine per 100 Cc., Mg.	Acetone Plus Diacetic Acid of Blood per 100 Cc., Mg.	Blood Sugar per 100 Cc., Mg.	Convulsive Seizures	Comment
12:05 p.m.	123.6	5.4	96	None for week except for two mild ones 3 days previously from break in diet	Diet: protein, 32 Gm.; fat, 200 Gm.; carbohydrate, 28 Gm. Being taken well
4:30 p.m.	190.3	6.9	70		
6:00 p.m.	Given meal of 200 Gm. carbohydrate				
6:30 p.m.	Given 20 units of insulin subcutaneously				
8:30 p.m.	Given approximately 75 Gm. more carbohydrate				
7:25 p.m.	42.8				
9:05 p.m.	1.9				
11:20 p.m.	1.8	0.9	108	At 12:20	Mild glycosuria
12:35 a.m.	2.6	0.8	108	severe	
1:55 a.m.	2.0				
2:15 a.m.	Qualitative tests	...	..	At 2:05	Attack mild
3:05 a.m.	negative	...	..	At 2:45	Moderately severe

notwithstanding the fact that the total ketone output for this twenty-four hour period was considerably greater than that for any equivalent period following it, when seizures did not occur. In our experience with the ketogenic diet in the treatment of patients with idiopathic epilepsy, we have often seen a latent period also between the time of disappearance of the ketosis and recurrence of seizures. A good example of the latter tendency is shown by one of the cases studied by Talbot, Metcalf and Moriarty.[17] The patient referred to had been having from forty to eighty seizures daily before they were brought under control, but she did not have any thereafter during the ketogenic diet period. When the diet was changed abruptly to one high in carbohydrate, the patient remained free from convulsions for three days following the change and had only one attack daily for the two following days, although the excessive amounts of acetone bodies had disappeared from the urine by

17. Talbot, Metcalf and Moriarty (footnote 3, second part, p. 224).

the end of the first day of the new diet. With less severe cases, the period of freedom from attacks, following disappearance of the ketosis, is usually much longer.

The acute experiment recorded in table 6 was made to determine the minimal duration of the latent period under special conditions. The degree of ketosis at the beginning of the experiment was marked, as indicated by the concentration of acetone bodies in both the blood and the urine. We feel certain from our experience with this particular patient that she would have remained free from seizures almost indefinitely had this level of ketosis been maintained. For the purpose of abolishing the ketosis rather suddenly, the patient was given at 6 p. m. a meal containing 200 Gm. of carbohydrate, with a minimal amount of protein and no fat. One-half hour later, 20 units of insulin was given subcutaneously to accelerate, if possible, the rate of the ketolytic processes. At 8:30 p. m., an additional 75 Gm. of carbohydrate was given. The blood sugar and the concentrations of acetone bodies in the blood and the urine were determined at intervals, as shown in the table. By 9:05 p. m., the concentration of acetone bodies in the urine had fallen even below that in normal urine, and to one one-hundredth of what it was at 4:30 p. m. The first convlusion occurred six and one-third hours after the first carbohydrate was given, which demonstrates that the latent period is not necessarily one of days. The fact that the blood sugar values were elevated slightly above normal shows that the convulsions were not due to hypoglycemia caused by insulin. The experiment demonstrates again that a definite relationship exists between the degree of ketosis and the occurrence of convulsions. It will be observed, however, that the convulsions did not come on immediately after the ketosis had entirely disappeared, as they frequently do in the case of hypoglycemia from insulin, but that there was a delay of at least three hours. The reason for this delay, as for that referred to as occurring in the less acute experiments, is obscure. Further work is being done on this phase of the problem.

COMMENT ON THE KETOGENIC DIET

The degree of ketosis required for the prevention of epileptic seizures differs greatly with different patients, and probably varies in the same person from time to time, according to a number of factors. This variability indicates the necessity for adjusting the diet of the individual patient in a way that will insure the optimum degree of ketosis for control of his disorder. Harmful effects from prolonged use of strongly ketogenic diets have not yet been reported. Still, it would not, apparently, be of advantage at present to maintain extreme degrees of ketosis in the milder cases in which control is possible with the less strongly ketogenic diets.

As regards the essential constituents of the diet, it may be safely assumed from the recent work of Bartlett [18] that the protein requirement of children beyond the age of 2 years on otherwise adequate diets is not more than 1 Gm. per kilogram of body weight. Even in the presence of ketosis, this amount has been found adequate for growth by Talbot and his co-workers.[19] If a satisfactory degree of ketosis is to be developed, the amount of carbohydrate frequently must be considerably less than 1 Gm. per kilogram of body weight, especially in older children and in those with severe epilepsy. The amount of fat to be prescribed is that which is necessary to complete the person's total energy requirement. Of course, when the patient is obese and reduction in weight is desirable, a smaller amount of fat should be allowed in the diet in order to force utilization of body fat; or, if he is undernourished and will take extra fat, this may be given without important change in the degree of ketosis, so long as the amounts of protein and carbohydrate are kept within certain limits.

The method which we have adopted as a starting point in the calculation of our ketogenic diets is as follows: Children up to the age of 5 years are allowed 1.25 Gm. of protein and 0.75 Gm. of carbohydrate per kilogram of body weight. Those between 5 and 10 years are given 1 Gm. of protein and 0.5 Gm. of carbohydrate, while those above 10 years receive 1 Gm. of protein and 0.25 Gm. of carbohydrate per kilogram. The remainder of the caloric requirement is made up from fat. In estimating the total energy required in the diet of a patient, the basal metabolism, as predicted from the standards of Benedict and Talbot,[16] plus a 50 per cent allowance for specific dynamic action, muscular activity and growth, is taken as a general guide. This is then modified to meet special requirements as they present themselves.

When the protein is limited to 1.25 Gm. and the carbohydrate to 0.75 Gm. per kilogram of body weight, as for preschool children, the amount of fat to be given is conveniently calculated from the simple equation:

$$\text{Fat (Gm.)} = \frac{1.5\ (\text{calories of basal metabolism for 24 hours}) - 8\ (\text{Kg. of body weight})}{9}$$

For patients between the ages of 5 and 10 years, who are allowed 1 Gm. of protein and 0.5 Gm. of carbohydrate per kilogram, the fat is calculated from the equation:

$$\text{Fat (Gm.)} = \frac{1.5\ (\text{calories of basal metabolism for 24 hours}) - 6\ (\text{Kg. of body weight})}{9}$$

For older children between 10 and 15 years of age, whose diets are limited in protein to 1 Gm. and in carbohydrate to 0.25 Gm. per kilogram of body weight, the fat is calculated from an equation only slightly different:

$$\text{Fat (Gm.)} = \frac{1.5\ (\text{calories of basal metabolism for 24 hours}) - 5\ \text{Kg. of body weight})}{9}$$

18. Bartlett, W. M.: The Protein Requirement as Determined in Diabetic Children, Am. J. Dis. Child. **32**:641 (Nov.) 1926.

19. Talbot, Metcalf and Moriarty (footnote 3, first part).

When typical diets for any age are calculated on this basis and the proportions of total available fatty acid and glucose are compared, it becomes apparent that the ketogenic to antiketogenic ratio is always above 3.2:1, which insures ketosis of a fairly marked grade. The younger the patient, the greater is the ratio in this calculation, because of the higher basal metabolism. This makes it possible to give the younger children slightly more protein and carbohydrate per unit of body weight, than the older ones for production of the same degree of ketosis.

The desirability of starting the ketogenic diet with relatively small amounts of fat and gradually increasing the quantity as the patient becomes accustomed to it has been properly emphasized by various persons. It has been our experience that the diet as calculated here is taken immediately without objection, when preceded by a fasting period of two or three days. Since the effect of the preliminary fast is to hasten the production of ketosis and to abolish in part the marked downward swing in the degree of ketosis during the postabsorptive period, this procedure recommends itself, particularly in the more severe cases. Even when the fast is employed, however, it is often well to give only half of the calculated quantities of protein, carbohydrate and fat on the first day of the diet. One of the most common reasons for the patient's sickening of the concentrated high fat diet is that its total caloric value is made to exceed his requirements too greatly. In addition to avoiding this error, one must, of course, aim to make the diet palatable and entirely complete as regards its vitamin and mineral content. In a small number of cases it may be desirable to give a midnight meal to prevent the morning decrease in ketosis shown in the preceding charts.

SUMMARY

The variations during the day in the rate of excretion of acetone bodies have been determined in a series of normal and epileptic children on ketogenic diets. When the diet was entirely consumed in either three or four equal meals at five hour intervals, variations in the intensity of ketonuria were found to describe a characteristic curve with its peak in the late afternoon and its lowest level during the hours between 3 and 9:30 a. m. The increase in the rate of excretion to its maximum point during the early hours of the absorptive period was rapid, compared to the gradual fall to the minimal level during the night. When four meals instead of three were given, the decline in the curve was interrupted by a secondary rise following the last meal. A difference was not observed between the curves for normal and epileptic subjects, when the conditions were the same. Although there was a definite increase in the afternoon in the rate of excretion of acetone bodies by persons on borderline diets, the curve of excretion for those on high carbohydrate rations did not show any such tendency.

The effect of preliminary fasting on the variations in the excretion of acetone bodies from use of the ketogenic diet has been shown to be that of greatly lessening the difference between the high and the low levels for the day. The explanation assigned for this is the depletion of the stores of glycogen by the fast. A temporary storage of small amounts of glycogen was assumed to take place during the absorptive period, however, in the case of an obese child previously on a ninety hour fast, notwithstanding the facts that the ketogenic to antiketogenic ratio of the diet was 2.9:1, and the total caloric value below her requirements. It has been assumed that utilization of this glycogen during the morning hours accounts in large part for the decrease in acetonuria at that time.

When an epileptic subject on a ketogenic diet was permitted to develop a degree of ketosis just below that necessary to prevent convulsive seizures, she was observed to have practically all of her attacks during the morning hours, at the time when the ketonuria was minimal for the day. As soon as the morning level of ketosis was raised well above a certain point, convulsions ceased to occur.

The convulsions observed in the morning under the conditions described were shown not to be caused by hypoglycemia. The direct relationship between the degree of ketosis and the freedom from epileptic seizures was shown in one acute experiment, in which convulsions followed the sudden abolition of ketosis in a few hours.

The rationale of the ketogenic diet, as used in the treatment of epilepsy, is discussed, and a plan is suggested for calculating a diet which will insure ketosis.

CONCLUSIONS

1. When the ketogenic diet is given to children during the day, in three or four equal meals, there is a characteristic curve of excretion of the acetone bodies with a high peak in the afternoon and a low level in the morning hours.

2. As there appears to be a direct relationship between the degree of ketosis and the effectiveness of the diet in preventing epileptic seizures, the wide variations in the degree of ketosis indicated by this curve probably account for many apparent failures in this form of treatment. To be satisfactory, the diet must be so adjusted that the minimal level of ketosis for the day is raised well above the threshold at which seizures occur.

3. The diet must be adjusted for each person to meet his particular requirements, as regards: (*a*) the necessary degree of ketosis to prevent attacks, (*b*) total caloric value, (*c*) protein and vitamin content and (*d*) digestibility and taste.

4. A preliminary fast of a few days tends to insure the success of the ketogenic diet.

ERYSIPELAS

A CLINICAL STUDY OF THE TREATMENT OF THIS DISEASE *

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During the past ten years, the treatment of erysipelas has been the subject of repeated investigation and discussion. The World War, no doubt, was a big factor in bringing this about, as erysipelas was a common and severe complicating factor of infections in wounds.

The discovery that light had physicochemical potentials which were extremely active and which evidently had powerfully potent therapeutic possibilities naturally led to the thought that this agent could be useful in the treatment of a patient with a condition such as erysipelas.

Again, more recently, the immunologic studies of diphtheria and scarlet fever and the great advances, from a diagnostic and therapeutic standpoint, made in the treatment of patients with these conditions have led investigators to attempt similar therapeutic procedures in erysipelas.

Although it is well recognized that erysipelas is definitely a self-limited disease and that it does not ordinarily present a serious problem in the older child and adult, if properly managed, it has always continued to be a formidable and extremely grave infection in the young, the aged, the puerperal mother, and as a complication of extensive infection in wounds.

The many forms of treatment that have been advocated from time to time and particularly extolled, such as treatment with phenol, the use of alcohol alone, of solutions of magnesium sulphate or of tincture of iodine, and many other types of treatment, have all failed at crucial times in the severe case and are at best never characterized by the assurance of certain and rapid relief. The good results reported by transfusion are evident, but the procedure is not as practical and safe as other methods.

The earliest reference to the use of light in the treatment of erysipelas is by Finsen,[1] who used carbon arc red light much in the

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* From the Department of Pediatrics, University of Minnesota, and the Contagious Wards of the Minneapolis General and Ancker Hospitals.

* Read before the Section on Diseases of Children, American Medical Association, Washington, D. C., May, 1927.

1. Finsen, N. R.: Behandling af rosen med udelukkelse af dagslysets kemiske straaler, Medd. f. Finsens med. Lysins. **4**:108, 1902.

same manner as he did in the treatment of variola. The result was not striking. He also felt that the favorable results reported by Kruckeberg [2] should be viewed with skepticism.

Some years after Finsen's report, Aristide [3] reported thirty cases in which the patients were treated with carbon arc red light. All cases were of the severe types; three of them occurred in infants. He was much impressed with his results. The duration of the disease was shortened, and the general condition was unmistakably improved.

A similar favorable report is given by Müller,[4] who used this form of treatment in sixty cases. It is difficult, however, to agree with him in view of his statement that the improvement in the patients was gradual.

The more accurate analysis of the solar spectrum, particularly with reference to the photochemical activity of the various rays and the recognition that some of them, notably the infra-red and the ultraviolet, could materially influence and alter the living cell led to the extensive use and application of this form of light in the treatment of disease.

Its possibilities in tuberculous skin conditions and in superficially located suppurating wounds, in glandular, joint and other forms of tuberculosis, have been pointed out by Finsen, Rollier and many other observers.

Reports of treatment for erysipelas with ultraviolet ray began to appear in 1916, although Koenig [5] used it as early as 1913. He was not particularly impressed with the effectiveness of the treatment and not only noted failures in his cases, but also had the definite impression that in some patients the condition grew worse following treatment. He ascribed this to the pronounced hyperemia which commonly occurs as a result of the irradiation.

Other writers, notably some military surgeons of the Central powers, Beck,[6] Carl [7] and Capelle,[8] report excellent results in the treatment of severe infections in wounds. Even severe processes were checked rapidly, with corresponding improvement in the patient's general con-

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2. Kruckeberg, H.: Rev. internat. de thérap. phys. (Feb.) 1902.

3. Aristide, S.: Fototerapia este cel mai eficace tratament al erisipelului, Spitalul. **31**:1, 1911.

4. Müller, O.: Die Behandlung des Erysipels mit Rotlichtbestrahlung, München med. Wchnschr. **64**:348, 1917.

5. Köenig, F.: Behandlung des Erysipels mit Quartzlampenbestrahlung, München med. Wchnschr. **63**:1701, 1916.

6. Beck, K.: Zur Behandlung des Erysipels, München med. Wchnschr. **63**: 892, 1916.

7. Carl, W.: Die Quartzlichtbehandlung des Erysipels, Deutsche med. Wchnschr. **42**:595, 1916.

8. Capelle, W.: Erysipelbehandlung mit künstlicher Höhensonne, Ztschr. f. Chir. **32**:658, 1916.

dition. This improvement often takes place after the first exposure. It was their contention that a considerable margin of healthy skin beyond the margin of the diseased skin must also be irradiated. They believe that the exposure should be given daily and should continue two days after the cessation of all symptoms. It was recommended that the area to be treated should be 1 meter from the lamp and that the average duration of the irradiation should be of ten minutes.

In 1919, Schenck-Popp [9] reported a series of eighteen cases in which the patients were treated with the mercury vapor quartz lamp; included among them were four infants between 8 and 14 days of age, and eight infants between 2 and 4 weeks of age. The treatment seemed to be efficacious in all superficial lesions, but failed when the infection was extensive and involved the blood or lymph channels. A few years later, Petenyi,[10] reported fourteen cases in infants, five of them newly born. All of the latter developed the lesion about the umbilicus, and two infants died; the others showed a striking improvement after the treatment.

Shortly after this, Czepa [11] reported his results in 100 cases. In nearly 100 per cent of his cases, improvement, such as fall in temperature and cessation of extension of the process, occurred after the first exposure. A similar favorable report is given by Brünauer. [12]

There are few references in the literature to the treatment of erysipelas with the roentgen ray. In 1915, Magelhaes,[13] a Brazilian physician, used it with striking success in a case of erysipelas complicating carcinoma of the face. He himself contracted erysipelas and was successfully treated. He subsequently reports nine more cases, several of them refractory and recurrent types of erysipelas. The roentgen-ray treatment seemed to be unusually effective. In 1917 and 1918, Schmidt [14] and Hesse [15] reported twenty-eight and forty-three cases, respectively, in which the patients were treated by roentgen ray Their results with this form of treatment were favorable. Most of the

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9. Schenck-Popp, H.: Künstlicher Höhensonne bei Erysipel u. anderen Infektionen im Säuglingsalter, München med. Wchnschr. **66**:557, 1919.

10. Petenyi, G.: Ueber die Quartzlampenlichtbehandlung des Sauglings Erysipels, Monatschr. f. Kinderh. **21**:269, 1921.

11. Czepa, A.: Zur Behandlung des Erysipels mit der Quartzlampe, Wien. klin. Wchnschr. **35**:564, 1922.

12. Brünauer, S. R.: Zur Behandlung des Erysipels mit ultravioletten Licht, Med. Klin. **29**:1003, 1924.

13. Magelhaes, J. A.: Du traitement de l'érysipèle par les rayons X, Mém. Acad. nationale de méd. de Brésel, May 21, 1916; Pará Medico 1917, vol. 1.

14. Schmidt, A.: Behandlung des Erysipels mit Roentgenstrahlen, München med. Wchnschr. **64**:1144, 1917.

15. Hesse, W.: Die Behandlung des Erysipels mit Roentgenstrahlen, München med. Wchnschr. **65**:505, 1918.

patients showed marked improvement after the first or second exposure, as evidenced by abrupt fall in temperature, cessation of edema and marked improvement in general.

Heidenhain's [16] results, published during the past year, were not so favorable. He treated thirty patients who had erysipelas of the face and scalp by roentgen-ray irradiation. In twenty, there was marked benefit. He ascribed his mediocre results to the use of too weak a dosage.

Within the past two years, Birkhaug [17] has proposed a specific antitoxin for erysipelas, which is prepared in a manner similar to that used in making antitoxin for diphtheria and scarlet fever. Birkhaug [18] has more recently used the toxin from *Streptococcus erysipelatis* for active immunization. This has a concentration of between 5,000 and 10,000 skin test doses per cubic centimeter. He has also found that during the acute stages of erysipelas, the patient's skin reacts positively with ten skin test doses of specific streptococcus toxin. Within about ten days, this skin reaction becomes negative simultaneously with the disappearance of toxin from the patient's blood. With this disappearance of toxin from the patient's blood, a progressive increase of antitoxin appears in the serum which is capable, in proper mixture, of completely neutralizing any toxin produced by *Streptococcus erysipelatis*. This active immunity conferred on the patient by an attack of erysipelas generally disappears in about six weeks. A negative skin test will again become positive, and the patient is subject to a recurrence of the condition.

Birkhaug has succeeded in producing a rapidly increasing concentration of antitoxin in the patient's blood through biweekly injections (intramuscular) of 500, 5,000 and 50,000 skin test doses of extracellular and intracellular toxin produced by *Streptococcus erysipelatis*. This treatment seems to give great promise in the prevention of recurrence of erysipelas.

In the present study, the therapeutic value of roentgen ray and antitoxin is considered particularly. The observations were made in eighty cases (table 1) in which the patients were treated by roentgen-ray irradiation, and on thirty patients (table 2) to whom antitoxin was administered. In addition, an analogous group of thirty-five unselected patients treated with magnesium sulphate and glycerin packs (table 3)

16. Heidenhain, L.: Roentgenbestrahlung in Entzündung, Strahlentherapie. **24**:37, 1926.

17. Birkhaug, K.: Erysipelas: V. Observations on the Etiology and Treatment with Erysipelas Antistreptococcic Serum, J. A. M. A. **86**:1411 (May 8) 1926.

18. Birkhaug, K.: Erysipelas: VI. Immunization with Soluble Toxin from Streptococcus Erysipelatis Against Recurrent Attacks of Erysipelas, J. A. M. A. **88**:885 (March 19) 1927.

was used as a control. The eighty cases in which the patients were treated by the roentgen ray include twenty-three previously reported by one of us (Platou [19]).

The technic of the roentgen-ray treatment as evolved by Dr. Rigler, roentgenologist at the Minneapolis General Hospital, is as follows:

Cases of erysipelas of the face were divided into four areas of exposure: one anterior, over the face and forehead; one on each lateral surface of the face and neck, including the ear; one on the scalp. The first three areas were always treated regardless of whether they were all involved or not, in the hope

TABLE 1.—*Data Obtained from Eighty Patients with Erysipelas Treated by Roentgen Rays*

Age	Duration at Time of Treatment, Days	Temperature	Degree of Infection	Time from Treatment to Normal Temperature, Days	Time to Normal Symptoms, Days	Extension After Treatment	Deaths
12 weeks to 84 years *	1 to 28	98.6 to 106 F.	15 mild 30 moderate 35 severe	½ to 9	1 to 6	17	5
37 †	4.4	.....	.....	1.5	2.01	24%	6%

Range.* Average.†

TABLE 2—*Data Obtained from Thirty Patients with Erysipelas Treated by Antitoxin*

Age	Duration at Time of Treatment, Days	Temperature	Degree of Infection	Time from Treatment to Normal Temperature, Days	Time to Normal Symptoms, Days	Extension After Treatment	Deaths
2 months to 78 years *	1 to 7	99 to 105 F.	4 mild 10 moderate 6 severe	1 to 2	1 to 8	14	2
41 †	3.2	.....	.....	2.2	3.9	46%	6%

Range.* Average.†

of preventing a spreading of the disease to the normal areas. The area over the scalp was treated only when invasion was in process or invasion was threatened. Protection was used only over the eyebrows. A distance of 10 inches (25.4 cm.) from the tube to the skin of the patient was used over all the areas, with 2 mm. of aluminum as a filter. The readings were 111 kilovolts (peak), corresponding approximately to a 7 inch (17.7 cm.) spark gap between moderately blunt points, and 5 ma. for five minutes over each area. This was considered a dosage sufficient to produce a mild erythema when the oblique radiation from each area was taken into account. The duration of the dosage over the scalp was reduced to four minutes to avoid any possibility of producing permanent epilation. Only one treatment was given, all the areas being exposed on one occasion.

19. Platou, E. S., and Rigler, L.: Roentgen-Ray Therapy in Erysipelas, Arch. Int. Med. **38**:573 (Nov.) 1926.

In the cases of erysipelas in other parts of the body, the affected area, together with a large border of normal skin around it, was treated in the same way, the part to be treated being divided into contiguous areas of approximately 300 sq. cm.

On comparing the results in patients treated by the roentgen ray (table 1) with those treated with local applications (table 3), it is noted that the average age of the control group is 40 years, of which only five patients were less than 3 years of age. The average age of the patients treated by the roentgen ray was 37 years, and ten patients were under 3 years of age. Among the thirty-five persons in the control group, including only five children under 3 years of age, there were eight deaths (23 per cent mortality), whereas among the eighty irradiated patients, ten of whom were below 3 years, there were only five deaths (6 per cent mortality). It is noteworthy that in the group of patients treated by roentgen ray only 50 per cent of the infants and none of the

TABLE 3.—*Data Obtained from Thirty-Five Patients with Erysipelas Treated by Iced Magnesium Sulphate and Glycerin Packs*

Age	Duration at Time of Treatment, Days	Temperature	Degree of Infection	Time from Treatment to Normal Temperature, Days	Time to Normal Symptoms, Days	Extension After Treatment	Deaths
4 weeks to 70 years *	1 to 32	98 to 104.2 F.	9 mild 14 moderate 13 severe	2 to 30	2 to 38	24	8 { 4 infants 4 adults
40.4 †	4.0	.....	.....	3.4	8.02	69%	23%

Range.* Average.†

adults died, whereas in the control group, 80 per cent of the infants and four adults died. This observation suggests that although roentgen-ray treatment is not as efficacious in infantile erysipelas as in the adult type, it is far better than local applications.

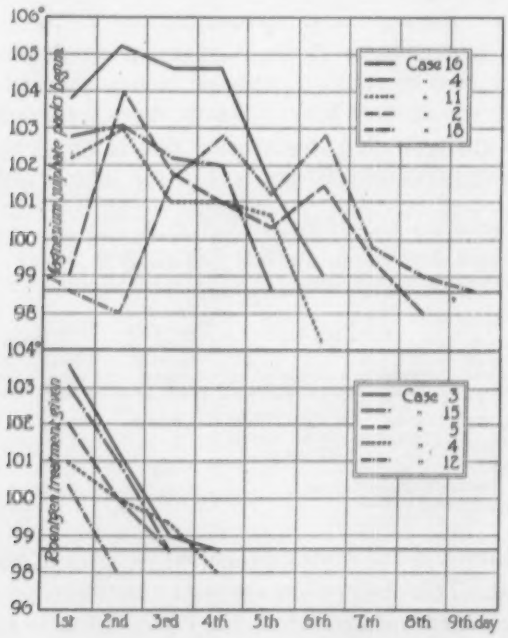
The average duration of illness at the time treatment was instituted was about the same in the two groups, but the average time elapsing between treatment and a return to normal temperature in the controls was 3.4 days, while in the patients treated by roentgen ray it was only 1.5 days. The average duration of symptoms, (pain, toxicity and general malaise) was about 8 days in the subjects in the control group and only 2 days in those treated by roentgen ray. Twenty-four (or 68 per cent) of the thirty-five persons in the control group showed rather marked extension of the disease as compared with seventeen (or 21 per cent) of the eighty patients treated by the roentgen ray.

In order to present graphically the comparison between control and irradiated patients from the point of view of temperature, the observations in ten cases are reproduced as in a previous report in the accompanying chart. Five of these are subjects from the control group

and five from the patients treated by roentgen ray. The cases are similar in regard to the age of the patients and the duration and extent of the infection.

ERYSIPELAS ANTITOXIN

With the standardization and acceptance of Birkhaug's antitoxic serum, its use in the hospitals of Minneapolis and St. Paul was soon begun, and to date we have records of the cases of thirty patients to whom it has been given.



Comparative temperature charts of five average patients treated with magnesium sulphate packs and of five average patients treated with roentgen rays. The unirridated cases are shown above; the irradiated cases are shown below; the highest temperature only is recorded for each day; the record is begun on the day when treatment was first given and ended on the first day of normal temperature; the lower temperatures and shorter temperature period of the irradiated patients is well shown.

The results obtained with its use were carefully tabulated on the same clinical data charts as were used for the control groups and for the patients treated with the roentgen ray; they are averaged and recorded in table 2. On comparing table 2 (serum cases) with table 3 (the control cases), it is evident that erysipelas antitoxin has real merit, and this confirms the impression we gained when we saw patients improve after its use. The inadequacy of a single therapeutic dose for adults, however, was soon apparent, and at present we advocate the

injection of from one to four such doses intramuscularly, depending on the age, extent, severity and duration of the disease.

In table 2 (serum cases) the average age was about the same as in the control group. Four of the thirty patients treated with serum were less than 3 years of age. As already noted, four of the five infants and four adults among the thirty-five control cases died (23 per cent mortality). Of the thirty patients treated with antitoxin, one of the infants and one adult died (total mortality 6 per cent). The average time elapsing between treatment and the return to normal temperature was 3.4 days in the control group, compared to 2.2 days in the group that was given serum; the duration of symptoms was eight days in the control group, compared to 3.8 days in the patients that were given serum. Sixty-eight per cent of the control group showed rather marked extension as compared to 46 per cent in the antitoxin series.

In order to facilitate comparison, the averages derived from the individual data in tables 1, 2 and 3 are combined in table 4.

TABLE 4.—*Average Data Obtained from 145 Patients with Erysipelas Treated by Local Applications, Roentgen Ray and Antitoxin*

	Control Group 35 Cases	Roentgenray Group 80 Cases	Antitoxin Group 30 Cases
Average age	40 years	37 years	41 years
Average duration	4 days	4.4 days	3.2 days
Average time from treatment to normal temperature	3.4 days	1.5 days	2.2 days
Average time from treatment to normal symptoms	8 days	2 days	3.8 days
Average percentage appreciable extension	68%	21%	46%
Mortality	23%	6%	6%

ANTITOXIN AND THE ROENTGEN RAY

Appreciating the failures encountered by all methods of treatment in some of the patients with severe cases of erysipelas, particularly in those occurring at the extremes of life, we have more recently used a combination of the roentgen ray and antitoxin. Although the series so treated is relatively small, the results in these few severe cases have been sufficiently gratifying to prompt a brief report of them.

PROTOCOLS

CASE 1.—B. R., aged 4 weeks, had erysipelas on the left arm and hand. The temperature returned to normal in twelve hours, and the erysipelas disappeared in two days.

CASE 2.—R. M., aged 2 years, had a mastoid wound with toxic erysipelas spreading over the face and scalp. The condition cleared up in ten days.

CASE 3.—G. H., aged 44 years, had erysipelas over the entire head, neck and arm, spreading down the back toward the hips. The patient was irrational for five days. The temperature was 105. Treatment was repeated, and the patient recovered in fifteen days.

CASE 4.—P. C., aged 44 years, had toxic erysipelas over the entire face and part of scalp. The patient was irrational. The condition continued to spread five days after antitoxin. The patient was given roentgen-ray treatment and recovered in ten days.

CASE 5.—P. C., aged 3 years, had a mastoid wound on the right side with erysipelas spreading over the face. The patient was treated twelve hours after the onset, and the erysipelas disappeared in two days.

CASE 6.—A. V., aged 30 years, had erysipelas over the entire face. The temperature was 104. The patient did not complain after the fifth day and erysipelas disappeared in ten days.

CASE 7.—O. P., aged 78 years, had erysipelas over the entire face and the right ear. The rise in temperature and symptoms disappeared by the fifth day.

CASE 8.—M. A., aged 3 months, had erysipelas over the face, bilateral mastoid wounds and neck. The erysipelas disappeared by the sixth day. Bronchopneumonia and meningitis developed later and death followed.

CASE 9.—A. B., aged 6 weeks, whose mother had erysipelas on the arm and chest from three to five days previously, had a temperature of 105. Erysipelas appeared on the entire right arm, back and right leg. The patient was prostrated. Incision over the back was followed by serous oozing; no pus. One roentgen-ray exposure was followed by a drop of 3 degrees in temperature. Ten cubic centimeters of Squibb's antitoxin was given; the temperature dropped to 100. This was followed by absolute cessation of the extension of the process and by complete recovery on the fourth day.

CASE 10.—A. W., aged 21 years, had a severe form of erysipelas over both cheeks and forehead. The condition was spreading. The temperature was 104, but it returned to normal on the third day following roentgen-ray treatment, or four days after the administration of antitoxin. The symptoms had disappeared by the fourth day, and the erysipelas had subsided by the sixth day.

SUMMARY

1. The present paper is based on observation on 155 cases of erysipelas. Thirty-five persons in the control group were treated with local application, eighty with roentgen-ray irradiation, thirty with erysipelas antitoxin and ten with the roentgen ray and antitoxin combined.

2. The efficacy of the roentgen-ray therapy is demonstrated by the prompt return to normal temperature (1.5 days in irradiated group, as compared with 3.4 days in the control group), and the more rapid disappearance of symptoms such as pain, toxemia and general malaise (2 days in the group of patients treated by roentgen ray, as compared with 8 days in the control group).

3. Extension of the disease occurred less frequently in the irradiated group (21 per cent) than in the control group (68 per cent). Such extensions as did occur in the former group usually progressed slowly, were slight in extent and often developed as isolated areas not in contiguity with the original diseased area.

4. The mortality in the group of patients treated by roentgen ray (6 per cent) was only one fourth of that (23 per cent) in the control group, in spite of the fact that the former included twice the number of infants under 3 years of age that were included in the control group.

5. Erysipelas antitoxin reflected its value by the return to normal temperature and subsidence of symptoms in 2.2 and 3.8 days, respectively, as compared with 3.4 and 8 days, respectively, required for the control group.

6. There was less tendency of the disease to spread in patients treated with serum (46 per cent) than in those treated by local applications (68 per cent).

7. The mortality among the patients receiving erysipelas antitoxin (6 per cent) was about one fourth that recorded for the subjects in the control series.

8. Our observations indicate that antitoxin and roentgen-ray irradiation are both of definite value in the treatment of erysipelas. The roentgen ray seems to be especially effective in inhibiting a spread of the disease and also in promoting a prompt subsidence of temperature and alleviation of symptoms.

9. Successful results following the use of antitoxin and the roentgen ray combined in ten cases in which the prognosis was considered especially grave from the point of view of age of the patient and extent and severity of the disease, indicate that probably the best form of treatment available at the present time includes the intravenous, intraperitioneal or intramuscular administration of erysipelas antitoxin in adequate dosage, in addition to a proper (large) roentgen-ray irradiation of the involved area and the contiguous normal skin.

THE BACTERIOLOGY OF DRIED POWDERED MILK PREPARATIONS USED IN INFANT FEEDING*

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An investigation of the bacteriology of preparations of dried, powdered milk was undertaken in connection with the study of an epidemic of enteritis. This epidemic occurred in an institution in which infants received artificial feedings composed largely of dried protein milk.

The Bacteriology of the Preparations of Dried Milk

	Per Gram of Powder
Powdered Protein Milk, Sample 1:	
Green-producing streptococci	12,000
Hemolytic streptococci	700
Variety of spore-bearing bacilli sarcinae, staphylococci, gram-negative bacilli and lactic acid bacilli	75,300
Total number of bacteria	88,000
Powdered Protein Milk, Sample 2:	
Green-producing streptococci	30,000
Variety of spore-bearing bacilli, sarcinae, staphylococci, gram-negative bacilli, and lactic acid bacilli	50,000
Total number of bacteria	80,000
Powdered Casein:	
Green-producing streptococci	6,000
Variety of spore-bearing bacilli, gram-negative bacilli, sarcinae and staphylococci	8,000
Total number of bacteria	14,000
Powdered Whole Milk:	
This sample contained a rapidly spreading bacillus that made accurate counts impossible	
Powdered Modified Milk:	
Green-producing streptococci	10,000
Variety of bacilli, including gram-negative bacilli, spore-bearing bacilli and staphylococci	9,000
Total number of bacteria	19,000

Samples of preparations of dried milk in use in two institutions were obtained. Cultures were made from them in the following manner:

A previously unopened can of each preparation was unsealed, and 1 Gm. of the powder was weighed out in a sterile container, a sterile spatula being used for handling the powder. The gram of powder was suspended in 10 cc. of sterile broth. One cubic centimeter of the suspension was transferred by means of a sterile pipet to another tube containing 9 cc. of sterile broth. Successive dilutions were made up to

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* From the John McCormick Institute for Infectious Diseases.

1 : 10,000. One cubic centimeter of each dilution was plated out in plain agar to which sterile, defibrinated sheep's blood had been added. Control plates were made of the sheep's blood agar and broth, and all plates were incubated for forty-eight hours. At the end of this time, the control plates were sterile. The variety and number of bacteria found in the powdered milk preparations are shown in the table.

A feeding prepared at one institution from protein milk, sample 1, contained 22,000 bacteria per cubic centimeter of which 11,000 were green-producing streptococci.

A feeding prepared in the other institution from protein milk, sample 2, contained 9,000 bacteria in 1 cc. with 7,000 green-producing streptococci.

CONCLUSIONS

The presence of a variety of living bacteria, including streptococci, in preparations of powdered milk indicates that the methods of manufacture do not destroy the bacteria in the milk and that the bacteria remain viable in the powder.

The preparation of powdered milk feedings without boiling or pasteurization in order to avoid curdling allows the bacteria in the powder to persist in living form in the feeding.

TUBERCULIN TESTS IN CHILDREN

A COMPARATIVE STUDY OF HUMAN AND BOVINE TUBERCULIN *

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Robert Koch [1] succeeded in isolating the tubercle bacilli in 1882 and later definitely established it as the etiologic factor of the disease by means of animal experimentation. To Theobald Smith [2] belongs the credit for differentiating the types of the tubercle bacilli. Most authorities give 1898 as the date of this important observation. However, in 1896, before the Association of American Physicians, Smith mentioned the difference between the two types. His complete work was published in 1898. He designated the tubercle bacilli isolated from man as the human type and those isolated from cattle as the bovine type. His work remains today practically unchanged. These types have definite bacteriologic characteristics and differ widely in many respects. It was not until 1901 that Robert Koch finally admitted the existence of the bovine type, but stated that it was rarely found in human tuberculous patients.

Koch also observed that when the products of the tubercle bacilli were injected into animals, there were both local and general reactions. This he designated as the tuberculin test. The old or crude tuberculin as originally prepared by Koch is as follows:

> To a 5 per cent glycerin broth media, 0.5 per cent sodium chloride and 1 per cent dried peptone were added. The tubercle bacilli were then cultivated at a temperature of 38 C. At the end of six weeks, there was a pellicle-like growth. The culture was then filtered, the filtrate heated to kill all living tubercle bacilli, and then concentrated to one-tenth its volume, making a 50 per cent glycerin solution. In view of the fact that there is associated a certain amount of danger in filtering live tubercle bacilli, it is preferable first to heat the culture to kill the bacilli and then to filter it and the filtrate concentrated as described. It is with this heated concentrated preparation designated as old tuberculin (Koch, 0.7) that the diagnostic tuberculin tests are now performed.

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* Received for publication, June 25, 1927.

* From the Pediatric Department of the New York Post-Graduate Medical School and Hospital.

1. Koch, Robert: Berl. klin. Wchnschr., 1882.

2. Smith, Theobald: Trans. A. Am. Physicians **9**:75, 1896; J. Exper. Med. **3**:451, 1898.

In 1905, Denys [3] prepared a filtrate from a 5 per cent glycerin peptone bouillon culture of *Bacillus tuberculosis* filtered through a Chamberlain filter. Phenol, 0.25 per cent, was added to insure sterility. This preparation is unheated and corresponds to the unconcentrated and unheated tuberculin of Koch, but, not having been heated, it is said by Denys to contain important soluble and thermolabile secretory products of the tubercle bacillus.

In an article published in 1908, and in October of the same year, speaking at the Washington Congress on Tuberculosis, L. Detre [4] proposed a modification of Pirquet's tuberculin test. He stated that by using the unheated bouillon filtrate of both the human and the bovine types as prepared by Denys, simultaneously, it would be possible to determine not only the presence or absence of a focus but also which of the two types was the causative organism. Somewhat similar results

TABLE 1.—*Bacteriologic Difference of Tubercle Bacilli* *

	Bovine Type	Human Type
Morphology	Short—stubby—thin	Slender—long—straight curved
Growth on Glycerin Bouillon	Produces little or no acid; media neutral or slightly alkaline; difficult to cultivate and produces thin pellicle which does not ordinarily extend to the surrounding glass	Produces much acid; media acid; more easily cultivated; produces luxuriant pellicle with wrinkled surface and which extends out to the glass
Virulence with Guinea-Pigs and Rabbits	Virulent with extensive lesions—usually kills animals	Low virulence; produces mild and slow disease from which animal usually does not die
Cattle	Bovine type universal in tuberculous cattle	Questionable whether human type can produce disease in cattle
Man	Able to produce disease; is causative factor in from 4 to 10 per cent in children and about 0.3 per cent in adults	Practically universal in humans with tuberculosis

* Smith: Trans. A. Am. Physicians **9**: 75, 1893; J. Exper. Med. **3**: 451, 1898. Hiss and Zinsser: Bacteriology, p. 498. Fishburg, M.: Pulmonary Tuberculosis, 1922, p. 27. Calmette, A.: Brit. J. Tuberc. **17**: 15 (Jan.) 1923.

were obtained by Koopman,[5] Kretchmer,[6] Cattaneo,[7] Klose [8] and Synwoldt.[9] Heated tuberculin was used in several instances, and the percentage of predominant bovine reaction varied greatly.

Detre [4] stated that there is little difference between the concentrated heated bouillon of both the human and the bovine types. Clarke and Forsythe,[10] working with the heated tuberculin of both types, stated that in pulmonary tuberculosis both reactions are usually present and con-

3. Denys: Louvain, 1905.
4. Detre, L.: Wien. klin. Wchnschr. **21**:173, 1908.
5. Koopman: Med. Klin. **19**:1193, 1923.
6. Kretschmer: Deutsche med. Wchnschr. **47**:465, 1921.
7. Cattaneo, C.: Ztschr. f. Kinderh. **6**:506, 1913.
8. Klose, E.: Deutsche med. Wchnschr. **36**:2239, 1910.
9. Synwoldt: Deutsche med. Wchnschr. **46**:455, 1920.
10. Clarke and Forsythe: British M. J. **19**:1193, 1920.

clude that human and bovine bacilli are closely allied or, which is less probable, that both bacilli are usually present.

In attempting to differentiate the type of infection, Downing and Higgins [11] used Koch's old tuberculin for the human tuberculin test and the bovine bouillon filtrate for the bovine test. This probably accounts for the high percentage of predominant bovine reactions (reactions to only bovine bouillon filtrate, 15.9 per cent and 27.4 per cent in which the reaction was predominantly bovine). In comparing the bouillon filtrate with the heated tuberculin of the same type, Denys [8] found that the bouillon filtrate gave the greater reaction.

The difference of opinion as to the ability to differentiate the type of infection with tuberculin prompted us to investigate for ourselves.

INVESTIGATIONS

The intradermal (Mantoux) test was performed simultaneously on children, many of whom were known to have both surgical and pulmonary tuberculosis, with dilutions of either 1 : 1,000 or 1 : 100, depending on whether there had been a previous negative reaction with the 1 : 1,000 dilution. In doubtful reactions, both tests were repeated with the stronger dilution. At no time was one test made without the other type for comparison. Bloch [12] found that the intensity of the reaction varies sometimes with the general and nutritional conditions of the child. He found a difference in four weeks with the same type.

Our group includes a number of children who were receiving or who had received tuberculin therapy subcutaneously. Koch's old tuberculin, as prepared by the New York City Health Department, was used as the human type and bovine tuberculin (OT), as prepared by Mulford, was used. Both tuberculins represented their respective heated, concentrated types. Dilutions were made from fresh preparations the morning of the tests. The anterior surface of the forearms was used as the site, the usual technical preparation being followed. The bovine tuberculin test was performed on the right forearm and the human test on the left. Care was taken that the tests were made on the same levels of the forearms, as the intensity of the reaction will vary with the sensitiveness of the skin. Obviously equal amounts of tuberculin were injected into the skin — 0.1 cc. producing a bleb about the size of a small pea. In instances in which more tuberculin was injected into one side because of an unruly patient, a notation of poor technic was put on the chart, with a prediction that that type would show the predominant reaction, with unfailing success. In such instances and in others in which there

11. Downing, H. F., and Higgins, H. L.: Intracutaneous Tests with Human and Bovine Tuberculin, Am. J. Dis. Child. **31**:178 (Feb.) 1926.

12. Bloch: Munchen. med. Wchnschr. **67**:1062, 1920.

was a difference in the intensity of the reaction, the tests were repeated at a later date. They were read by a well trained disinterested third party at the end of forty-eight hours and a week.

DATA

Of a total of 208 children who were tested with the human and bovine types, 75 gave positive reactions to the tuberculin tests. This should not be interpreted as indicating the incidence of tuberculous infection in the normal school child, as many of the children were from the tuberculosis clinic and the baby wards. Evidently these figures would be much higher than the average. In seventy-three out of the

TABLE 2.—*Summary of Data*

Total cases	208
Total positive tests	75
DIAGNOSIS	
Pulmonary tuberculosis	41
Malnutrition	8
Tuberculous cervical adenitis	6
Cardiac	4
Asthma	5
Upper respiratory infection	2
Bronchitis	2
Tuberculous meningitis	2
Tuberculoma of brain	1
Congenital syphilis	1
Tuberculosis of the hip	1
Sinusitis	1
Lymphatic diathesis	1
Total	75
Positive and both equal	71
Human greater than bovine	0
Bovine greater than human	1
Positive human and negative bovine	1
Positive bovine and negative human	0
Both negative in presence of tuberculous infection with previous human positive	2
Total	75

seventy-five cases that showed a positive tuberculin test, the human and bovine reactions were equal. In only two instances was there a difference in the reaction. Fred N. gave a 4+ bovine and a 3+ human reaction. This was due to poor technic, for it is impossible always to inject exactly the same amount either because of an unmanageable child or because of a loss of tuberculin due to an ill fitting needle. For this reason, we believe that it is advisable to measure the amount injected by the size of the bleb. In a number of children in whom there was a difference in intensity, the tests were repeated and subsequently proved to be equal.

Fred N. moved out of the city, and we were unable to get him back for retests. Sylvia M., for some unknown reason, gave a positive human and a negative bovine reaction. In this case also, we were unable to get the patient back. She was in good health and had no evidence of

disease. We feel certain that if we had been successful in getting back these two patients for retests, we would have been able to show 100 per cent equal reactions. Discrepancies may also be due to the difference in potency and toxicity of the tuberculins, which may be due either to the age of the preparation or to the fact that it is impossible to prepare different preparations of the same or different types of equal toxicity. Tuberculin has yet to be standardized. Schuster [13] performed tuberculin tests on patients who had been operated on and found that they reacted differently to the same and different OT at different times.

REVIEW OF CASES

A clinical review of several cases will bring out many important points.

CASE 1.—Thomas K., aged 19 months, had old healed tuberculous cervical adenitis. His father and grandfather both had tuberculosis. The onset dated back to 6 months of age, at which time the infant was breast fed and was operated on for tuberculous cervical adenitis. There was no possibility for the infection to have been caused by the bovine type, and the history of contact clearly demonstrates infection solely by the human type. Here the bovine and human reactions were equal.

CASE 2.—Anthony R., aged 9 months, had tuberculous bronchopneumonia. His mother died of tuberculosis when he was 8 months of age. The definite history of contact with the improbability of bovine infection points toward a single infection with the human type. Here the bovine and human reactions were equal.

CASE 3.—Harry L., aged 8 months, had tuberculous central pneumonia. Autopsy revealed a central caseous mass surrounded with miliary lesions, a condition usually caused by the human type. Here the human and bovine reactions were equal.

CASE 4.—Mary C., aged 6 years, had tuberculoma of the brain. She died from a tuberculous meningitis. Autopsy revealed a tuberculoma also. Here the human and bovine reactions were equal.

CASE 5.—Irene S., aged 4 years, had tuberculosis of the hip, a condition usually caused by infection with the bovine type. There was no history of tuberculosis in the family. Here the bovine and human reactions were equal.

CASE 6.—John E., aged 3 years, had tuberculous cervical adenitis. The technic of the first reaction was poor, and the prediction was made that the human reaction would be greater than the bovine, which proved correct. A repetition of the tests revealed that both reactions were equal. This child was transferred to the surgical department. His tonsils were removed, and on microscopic examination tubercle bacilli were found.

CASE 7.—David N., aged 3 years, had miliary tuberculosis of the lungs and tuberculous meningitis. The human tuberculin test was performed on admission, and was positive. The patient grew steadily worse four days after admission. Both human and bovine tests were performed simultaneously, and both were negative. The patient died about a week later. If we had performed the bovine test only, we might have come to an erroneous conclusion. However, it was just

13. Schuster: Deutsche med. Wchnschr. **46**:1102, 1920.

a case of a negative tuberculin test in the presence of an overwhelming tuberculous infection.

CASE 8.—Fred C., aged 6 years, had asthma. A previous Mantoux test with a dilution of 1:1,000 of the human type was positive. He was receiving tuberculin (human type) for his asthmatic condition. Subsequent tests with 1:100 proved to be both positive and equal. This definitely proves a close relationship, at least, with the heated preparations between the bovine and human tuberculin, for human tuberculin desensitized not only this patient to the human type but also to the bovine type.

CASE 9.—Jacob G., aged 13 years, had asthma. His case emphasizes the same point as case 8. A previous Mantoux test with human tuberculin was positive. He then received tuberculin therapy, after which the Mantoux test was negative, with both human and bovine tuberculin, even with the more concentrated solution (1:100).

That we were unable to differentiate the type of infection with the heated concentrated tuberculin substantiates the works of Denys [3] and Detre.[4] There is no doubt that heated tuberculin undergoes a chemical change. In heating and concentrating the bouillon filtrate, there is a fatty albuminous foam on the surface. Detre restored this heated preparation (OT) to its original dilution and made comparative protein

TABLE 3.—*Data of Tuberculin Preparations*

Albumin Test	Unheated Filtrate	Restored—Heated Old Tuberculin
Potassium cyanide	+	—(Neg.)
Acetic Acid	Cloudy +	—(Neg.)
Nitric Acid	+	—(Neg.)

tests with the bouillon filtrate (unheated) of the same type. He used the K.C.N.—acetic acid and nitric acid tests.

In all these tests the original unheated unconcentrated bouillon filtrate gave a positive protein test, whereas the restored old tuberculin (the heated concentrated preparation) gave negative tests. He concluded that the more active toxic substances of tuberculin are thermolabile and are the true differential toxins which are attached to albuminous substances. Two possibilities present themselves:

1. That it is not possible to differentiate the type of infection with old tuberculin.

2. That it is possible to differentiate, but that there was a double infection in every one of our cases presenting positive reactions.

All evidences point against the second assumption. The possibility of a double infection in every case is extremely remote. Many of our cases show a definite history of human contact, and in three cases the age would preclude infection with the bovine type. In one case, the onset was at 6 months, at which time the child was being breast fed and the father and grandfather both had active tuberculosis. In two cases

in which the tuberculin tests were previously positive, tuberculin therapy with the human type desensitized them to both the human and the bovine types. If one assumes that there was a double infection, then tuberculin therapy with the human type desensitized the patient to both types, and if there was a single infection, subsequent tests with a more concentrated solution (1 : 100) should be made. Fred C. (case 8) proved that bovine and human tuberculins could give both positive and equal reactions. We have several such representative cases in which the patient, with a previous positive reaction to human serum of a 1 : 1,000 solution, had received tuberculin therapy; subsequent Mantoux tests (1 : 1,000 solution), with both human and bovine tuberculin, were negative, but with a 1 : 100 solution were positive and equal. In many of these cases, the reaction was not as marked as the previous positive one with the 1 : 1,000 solution.

Calmette,[14] subdirector of the Pasteur Institute, stated: "The bovine type bacillus is rarely met with in tuberculous lesions in man. Varying in different countries one finds them in from 4 to 10 per cent of the various types of tuberculosis in childhood and 3 per one thousand in chronic tuberculosis in adults." We can therefore justly assume that there was not a double infection in all our cases. Since there was not a double infection in all our cases and since in only two cases there was a difference in the equality of the tests, we must conclude that we were unable to differentiate the type of infection with old tuberculin.

Epstein [15] performed intracutaneous tests with the milk from tuberculous cows and confirmed the presence of tuberculous antigen in milk. He injected 0.1 cc. of milk into the skin of the forearms of children affected with tuberculosis who had given a positive reaction to tuberculin. As a control test, certified milk from nontuberculous cows and dried milk were injected into the other arm; a positive result was obtained in tuberculous children with milk of tuberculous cows, whereas a negative result was obtained with other milks on the same children. Further, the milk from tuberculous cows was injected into nontuberculous children with negative results. The injection of milk from tuberculous cows frequently caused a torpid Pirquet test to flare up and become markedly positive. The author concluded that the milk of tuberculous cows contains antigens not present in nontuberculous cows. This further emphasized the close relationship between the tuberculins of the human and bovine types, for it demonstrates the presence of a common antigen.

CONCLUSION

In view of the work of both Denys and Detre and because of our inability to differentiate the type of infection with heated concentrated

14. Calmette, A.: Brit. J. Tuberc. **17**:15 (Jan.) 1923.
15. Epstein, B.: Jahrb. Kinderh. **95**:64, 1921.

tuberculin, we advance the following hypothesis in explanation thereof. Both tuberculins contain a common antigen (B) which is theremostabile. (A) represents the differentiating thermolabile toxin for the human type, and (C) represents the differentiating thermolabile toxin for the bovine type. The unheated filtrate of the human type contains antigens (A + B) and the unheated filtrate of the bovine type contains antigens (B + C). In heating the preparations A and C, the thermolabile differentiating toxins of both types are destroyed, thus leaving the common thermostabile toxin (B).

However, it would be possible to differentiate the types of infection with the unheated filtrate. This procedure, we feel, is associated with too much danger in producing a tuberculous infection in which there was no infection and in activating the aquiescent lesion if one is present.

It is the concensus of opinion that there is a filterable virus present in the unheated preparation capable of producing an infection. Since the treament is essentially the same, no matter which type is the causative organism, we feel that it is a dangerous method and that the ends would not justify the means.

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Progress in Pediatrics

CONGENITAL ATRESIA OF THE COLON*

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Congenital occlusions of the colon are less common than those of the small bowel, and their gross anatomic characteristics have not been studied with the same thoroughness that characterizes the descriptions of occlusions of the small bowel and anus. In many of the larger text-books on morbid anatomy, pediatrics and surgery,[1] scant mention is made of atresia of the colon.

In recent treatises, Richter [2] and Grulee and Bonar [3] have thoroughly described the general characteristics of the malformations of the gastro-intestinal tract, and have summarized the theories so far advanced to explain the origin of occlusions of the gastro-intestinal tract.

In 1903 Kuliga [4] described twenty-three occlusions of the colon in 189 reports of congenital obstruction of the bowel. In Kreuter's [5] series of 194 congenital intestinal malformations, there were 33 of the colon. In 1912 Spriggs [6] reviewed 398 reports of congenital occlusion of the intestinal tract, and 20 of these were in the colon. In 1922, Davis,

* Received for publication, Aug. 5, 1927.

* From the Pathological Laboratories of the Presbyterian Hospital and the Norman Bridge Pathological Laboratory of the Rush Medical College of the University of Chicago.

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2. Richter, H. F.: Surgery of the Gastro-Intestinal Tract in Children, in Abt, I.: Pediatrics, Philadelphia, W. B. Saunders Company **3**:504, 1924.

3. Grulee, C. G., and Bonar, B. E.: The Newborn—Diseases and Abnormalities, New York City, D. Appleton & Company **3**:145, 1926.

4. Kuliga, P.: Zur genese der congenitalen Dünndarmstenosen und Atresien, Beitr. z. Path. Anat., u. z. allg. Pathol. **33**:481, 1903.

5. Kreuter, E.: Die Angeborene Verschliessungen und Verengerungen des Darmkanals im Lickte der Entwicklungsgeschichte, Deutsch. Ztschr. f. Chir. **79**:1, 1905.

6. Spriggs, N. I.: Congenital Occlusion of the Gastrointestinal Tract, Guy's Hospital Reports **66**:143, 1912.

Delmer and Poynter [7] reported thirty-nine cases of atresia of the colon among 392 occlusions of the gastro-intestinal tract. In none of these summaries, however, is a clear distinction made between microcolon and atresia of the colon, and the articles deal chiefly with the malformations of the small bowel. From a study of the reports of twenty-eight congenitally small colons, Greig [8] believes that many cases of so-called occlusions of the large bowel referred to in the literature have been inaccurately designated, because distinction has not been made between true congenital microcolon and secondary atrophy following occlusion of the small bowel.

The terms atresia, stenosis, occlusion and microcolon have sometimes been used interchangeably in medical literature to denote complete or partial diminution of the lumen of the large bowel. We have included as atresia of the colon only those with complete occlusion of the lumen resulting from changes in the wall of the large bowel. Many of the older studies on atresia of the colon, which did not contain adequate anatomic descriptions, have not been included in this review. Our case is typical in its clinical and anatomic characteristics of the majority of instances of atresia of the colon.

REPORT OF CASE

The following clinical and anatomic features may be regarded as typical:

History.—R. K., a white boy, was admitted to the service of Dr. Grulee at the Presbyterian Hospital, Chicago, on May 9, 1925, three days after an uneventful delivery at full term. Vomiting was present for forty-eight hours, and no meconium had been passed.

The child was acutely ill. The addomen was distended. Rectal examination revealed an obstruction about 4 to 5 cm. above the anus. The clinical diagnosis was congenital obstruction of the colon. Laparotomy was performed one hour after admission, and meconium was found in the peritoneal cavity, but the perforation of the bowel was not located. Death occurred two hours later.

Autopsy.—The anatomic diagnosis (C. W. A.) was atresia of the sigmoid portion of the colon; meconium-distended colon; spontaneous perforation of the cecum; acute serofibrinous peritonitis; free meconium in the peritoneal cavity; recent laparotomy wound.

The body was that of a full term white male child. The body was warm. The skeleton was symmetrical. Body nourishment was good. There was a recent surgical incision of the right lower quadrant of the abdominal wall, 5 cm. long, and a rubber drain protruded.

In the peritoneal cavity on the right side surrounding the cecum, there was green semifluid material resembling meconium. In the remainder of the peritoneal cavity there was turbid fluid, and the loops of the small bowel were

7. Davis, Delmer, L., and Poynter, C. W. M.: Congenital Occlusion of the Intestine, Surg. Gynec. Obst. **34**:35 (Jan.) 1922.

8. Greig, D. M.: Congenital Microcolon, Edinburgh M. J. **32**:175 (April) 1925.

Summary of the Important Gross Morbid and Clinical Alterations in Studies of Atresia of the Colon

Author and Date	Age and Sex	Location and Extent of Atresia of the Colon	Associated Gross Morbid Alterations	Cause of Death	Remarks
Smith: Lancet **1**: 794, 1840..	9 days F	Splenic flexure and part of descending portion, 22.5 cm. long	Colon ended in a blind sac; the next portion was obliterated for 22.5 cm. and the next portion was narrowed to the anus; the great omentum and appendix veriformis were absent	Unknown	No meconium passed; vomiting began at 30 hours; abdomen distended
Dawson: Am. J. Obst. **5**: 473, 1872	4 days ?	Middle of the transverse portion of the colon	Hypoplasia of the descending colon; dilatation and gangrene of the proximal end of the transverse portion of the colon	Acute peritonitis	No meconium passed; vomiting began on the second day
Anderson: Tr. Path. Soc. **42**: 128 1891	23 days M	Sigmoid flexure and rectum	Imperforate anus; the dilated colon ended in a conical blind extremity at the crest of the left ilium; the sigmoid flexure and rectum were entirely absent	Unknown	A fecal umbilical fistula developed one day after birth
Weiland: Med. News **68**: 44, 1896	2 days ?	Ileocecal valve and ascending portion of the colon	The ascending portion of the colon was absent; the upper fold of the ileocecal valve formed a membrane across the lumen	Unknown	Vomiting began 12 hours after birth; no meconium passed
Simmonds: München. med. Wehnschr. **47**: 170, 1900	Unknown	Sigmoid flexure	There was also atresia at the junction of the jejunum and ileum	Bowel obstruction	No meconium passed
Hepburn, Brit. M. J. **1**: 1264, 1902	2½ days ?	Descending portion of the colon from splenic flexure to the rectum	Occluded portion of the colon was a cord 3 mm. thick attached to the mesocolon; there was also atresia of the ileum	Unknown	No meconium passed
Fyfe: Brit. M. J. **1**: 250, 1903	23 days ?	Splenic flexure, descending and sigmoid portions of the colon	The transverse portion of the colon ended in a balloon-shaped sac; the rectum was patent	Inanition	No meconium passed; vomiting began on the second day
Clogg: Lancet **2**: 1770, 1904	6 days F	Ascending portion of the colon	Hypoplasia of the hepatic flexure and the distal portion of the colon; umbilical hernia in which ended lower part of small intestine	Unknown	Vomiting shortly after birth; distended abdomen; visible peristalsis
Jeanin and Cathala: Bull. Soc. d'obst. et de gynéc. de Paris **8**: 142, 1906	18 hours M	Descending portion of the colon	Spontaneous perforation of the colon distal to the splenic flexure	Acute peritonitis	No meconium passed; cyanosis at birth
Albers, cited by Kuliga: Beitr. z. path. Anat. u. z. allg. Pathol. **33**: 481, 1903	Unknown	Cecum and entire colon	Cecum, process veriformis and all of colon narrow; no lumen in a few places	Unknown	
Bednar, cited by Kuliga: Beitr. z. path. Anat. u. z. allg. Pathol. **33**: 481, 1903	5 days ?	Ascending portion of colon in region of right kidney by a membrane of mucosa	.....	Unknown	No meconium passed; thick mucus in large bowel
Nelaton, cited by Kuliga: Beitr. z. path. Anat. u. z. allg. Pathol. **33**: 481, 1903	Few days old ?	Beginning of ascending portion of the colon by a membrane of mucosa	Anus praeternaturalis	Unknown	
Mangoldt, cited by Kuliga: Beitr. z. path. Anat. u. z. allg. Pathol. **33**: 481, 1903	3 days ?	At junction of cecum and ascending portion of the colon	Atresia of rectum 5 cm. above anus.....	Unknown	

Smith, cited by Kuliga: Beitr. z. path. Anat. u. z. allg. Pathol. **33**: 481, 1903	30 hours F	Transverse portion of the colon	.....	Unknown	
Smith, cited by Kuliga: Beitr. z. path. Anat. u. z. allg. Pathol. **33**: 481, 1903	9 days ?	Descending portion of the colon	Large omentum and appendix veriformis absent; blind sac of the descending colon covered by peritoneum	Unknown	
Novicki, cited by Okinczye: Rev. de chir. **40**: 867, 1909	5 days ?	Ascending and transverse portion of the colon	Hypoplasia of the descending portion of the colon, sigmoid flexure and rectum	Unknown	
Goosman: J. A. M .A. **54**: 704, 1910	2½ days ?	Sigmoid flexure	Sigmoid flexure ended in a blind sac which lay along side of the upper end of the rectum; imperforate anus	Unknown	Vomiting began 12 hours after birth
Wilcox: J. M. A. Georgia **1**: 145 No. 4, 1912	2 days ?	Ileocecal valve to sigmoid flexure	Volvulus of the ileum; colon represented by a fibromuscular band	Unknown	No meconium passed; vomiting began 18 hours after birth; abdomen distended
Spriggs: Guys Hosp. Rep. **66**: 143, 1912	7 days M	Splenic flexure 22 cm. above anus	Membranous septum completely occluded lumen....	Unknown	No meconium passed
Spriggs: Guys Hosp. Rep. **66**: 143, 1912	4 days ?	Transverse, descending portion of the colon and rectum	Imperforate anus; stenosis of the ascending colon which ended in a blind sac; colon absent to anus	Unknown	No meconium passed; vomiting was persistent
Bonneau: Buil. Soc. d'obst. et. de gynéc. de Paris **4**: 466, 1912	3 days ?	Sigmoid flexure	Membranous atresia 10 cm. from anus.....	Acute peritonitis	
Mayer: Brit. M. A. **1**: 498, 1913	3 days F	Ileocecal valve to anus	Colon and rectum represented by a thin white cord with a transverse mesocolon and mesosigmoid; atresia of the ileum	Unknown	Vomiting on the second day
Jefferiss: Brit. M. A. **1**: 712, 1913	3 days ?	Cecum to the sigmoid flexure	Colon represented by a thin white cord.....	Unknown	First child had similar condition
Hyndman: J. Missouri M. A. **14**: 38, 1917	2 days M	Ileocecal valve	Hypoplasia of the colon; atresia of the rectum and volvulus of the ileum	Unknown	No meconium passed; vomiting began soon after birth; abdomen distended
Weidman: Proc. path. Soc. **21**: 5, 1918	6 days	Ascending portion of the colon for 15 mm. beginning 17 mm. from the ileocecal valve	Fibrous adhesions surrounding the ascending portion of the colon	Unknown	No meconium passed; abdomen distended; positive Wassermann test
Walker: M. J. Australia **1**: 216, 1919	1½ days	Descending portion of the colon, sigmoid flexure and upper part of rectum	Rectum ended within peritoneal cavity.....	Unknown	Distended abdomen
Walker: M. J. Australia **1**: 216, 1919	18 hours F	Cecum to upper part of rectum	Firm cord running up from occluded lower intestine to the abdominal wall and attached by rudimentary mesentery	Unknown	Abdomen distended and rectum patent
Gaug, 1922	M	Sigmoid flexure for 11.25 cm.	Absence of mesosigmoid.....	Recovered following operation	No meconium passed; abdomen distended; no vomiting
Farr and Fries: Surg. Clin. N. Am. **5**: 621 (April) 1925	8 days M	Junction of the sigmoid flexure and rectum	Occlusion of the ileum ?).....	Unknown	No meconium passed; distended abdomen, visible peristalsis; two other children died of same condition

adherent to one another by fibrin. The loops of the small bowel were collapsed. The transverse and ascending portions of the colon were markedly distended with meconium. The descending portion of the colon was also moderately distended and ended in a cone-shaped blind end at the left iliac crest, but was connected with the rectum by a fibrous cord, a part of the sigmoid portion of the colon which was 9 mm. in length and 0.5 mm. in diameter. Both the proximal and distal blind ends of the bowel were cone-shaped, the fibrous cord being attached at the apex of each cone. The mesosigmoid was from 3 to 4 cm. long, and there was no gross alteration in the part that was attached to the fibrous cord.

The circumference of the proximal blind end was 4.5 cm., and of the cecum 6.5 cm. The circumference of the distal blind end was only 11 mm. The lumen of the rectum enlarged toward the anus, where it was 2.3 cm. in circumference.

In the front wall of the cecum, 4 cm. from its tip, there was a perforation 2 cm. in diameter, its margins were thin, frayed and discolored, green-brown, for from 2 to 3 mm. The lymph follicles in the lining of the cecum and ascending portion of the colon were numerous, averaging 1 mm. in diameter, and about three to each square centimeter.

There were no gross malformations or alterations in the other organs of the body, except those associated with death from acute generalized peritonitis and distention of the abdomen.

THEORIES AND REPORTS

Several theories have been advanced to explain congenital atresia of the intestinal tract. Tandler [9] and Kreuter [10] found that the original lumen of most of the intestinal canal of vertebrates is lost in the early part of embryonic life by epithelial proliferation, but later is reestablished. In congenital atresia of the gastro-intestinal tract they, therefore, assumed that recanalization has not occurred. Bland Sutton,[11] however, maintained that occlusion of the alimentary tract always occurred at the site of an "embryological event," such as the junction of the rectum and anus, the ampulla of Vater, etc. Theremin [12] believed that intrauterine inflammatory diseases such as peritonitis and enteritis are followed by congenital occlusion.

Chiari [13] and others described healed intussusceptions and believed that this was a more common cause for congenital occlusions than is generally thought. Other factors that are frequently mentioned in explanation of occlusions of the bowel are disturbances in the supply of blood to the bowel as a result of vascular anomalies and embolism

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9. Tandler, J.: Zur Entwicklungsgeschichte des menschlichen Duodenum in frühen Embryonalstadien, Morphol. Jahrb., **29**:187, 1902.

10. Kreuter, E.: Zur Aetiologie der congenitalen Atresien des Darms und Oesophagus, Arch. f. klin. Chir. **88**:303, 1909.

11. Sutton, Bland: Imperforate Ileum, Am. J. M. Sc. **98**:457, 1889.

12. Theremin, E.: Ueber Congenital Occlusionen des Dünndarms, Deutsch. Ztschr. f. Chir. **8**:34, 1877.

13. Chiari, H.; Zur Entstehung der Congenitalen Darmatresia und Intussusception, Prag. med. Wchnschr. **28**:267, 1903.

or thrombosis of mesenteric vessels and of intra-uterine twisting of the intestine. With such a variety of etiologic factors, some partially confirmed by anatomic studies, it is reasonable to assume that no one cause can explain all of the occlusions. There were no anatomic alterations in the colon we examined that can be explained by one of the theories mentioned to the exclusion of the others.

The important gross anatomic and clinical alterations as a result of atresia in twenty-nine colons are described in the table. In seven, atresia occurred in the sigmoid flexure and rectum; in five, in the ascending portion of the colon; in three, in the transverse portion, and in two each, in the ileocecal valve, splenic flexure and descending portion. In eight instances, many of these portions of the colon were continuously occluded.

The most common alteration in congenital atresia is a replacement of a part of the colon by a nonpatent fibrous cord that connects the two patent portions. Usually the mesocolon is present, and the cord is attached to its free border. The proximal part of the bowel is distended and hypertrophied, the distal part is atrophic, and its lumen contains gray or brown inspissated mucus. In five cases, the lumen was interrupted only by a membrane of mucosa that stretched transversely from wall to wall.

The most common associated anomalies were occlusions of the small bowel; these were found, however, with atresic colons in only five cases. In three there was also an imperforate anus.

The cause of death was not mentioned in most reports. It results most commonly from acute generalized peritonitis subsequent to spontaneous rupture of the distended proximal part of the colon. Inanition and obstruction of the bowel are the other usual causes of death.

Clinical recognition, obviously, is simple in the absence of an imperforate anus. Meconium is not passed in the stool (occasionally inspissated discolored mucus forms a stool). The abdomen is usually distended. Vomiting begins in from twelve hours to several days after birth. Fluoroscopic examination usually demonstrates the location of the distal end of the obstruction.

Only one recovery [14] after surgical intervention is mentioned in the literature.

SUMMARY

One instance of congenital atresia of the colon is described, and twenty-nine cases of similar anomalies are reviewed.

Congenital atresia of the colon is uncommon. It can be recognized early clinically, but so far therapeutic measures have been successful in prolonging life only in one instance.

14. Gaug, O. C.: Congenital Stenosis and Atresia of Intestinal Tract Above Rectum with Report of Operated Case of Atresia of Sigmoid of Infant, Tr. Am. Surg. A. **40**:582, 1922.

News and Comment

AMERICAN MEDICAL ASSOCIATION OF BERLIN

The American Medical Association of Berlin has been reorganized and is acting as a central bureau of information for men seeking postgraduate work in Berlin. Five courses in pediatrics are offered. All except one of them are devoted largely to practical work and bedside clinics. The address of the Association is Berlin, N. W. 6, Luisenplatz, 2-4.

Abstracts from Current Literature

Anatomy and Physiology

A Method for Estimating the Size of the Thymus. F. O. Coe, Am. J. Roentgenol. and Radium Therapy **15**:222 (March) 1926.

By superimposing the shadows of arrows placed over the spinal of the vertebra and the midsternum, exact anteroposterior pictures were obtained. The smaller children were made to cry lustily and the picture was taken when the breath was held, so as to widen the thymic shadow by engorgement of the supradiaphragmatic organs and by elevation of the diaphragm. The measurement of the supracardiac shadow is 32 per cent of the transverse thoracic shadow at 3 months and averages about 35 per cent up to 20 months. It then declines to 30 per cent at 30 months and remains there up to 6 years and then gradually declines to 25 per cent at 8 years. Forty children between 8 and 12 years averaged 25 per cent. In contrast the curve of the enlarged thymus is 42 per cent at 2 months; it stays above 45 per cent until about the third year, when it descends to 40 per cent, remains there about two years and gradually declines to 32 per cent at about 7 years. The normal ratio of the supracardiac shadow to the internal transverse diameter of the chest, at the angle of Louis, is about 1:3, until the sixth year, and if this is found to approach or exceed 1 to 2, the thymus is enlarged.

The Roentgenographic Demonstration of the Trachea and Bronchi. P. M. Hickey and A. C. Furstenberg, Am. J. Roentgenol. and Radium Therapy **15**:227 (March) 1926.

In children, injection of iodized oil 40 per cent through the cricothyroid membrane by means of a curved trocar is preferred to either the supraglottic injection guided by the reflected image of the larynx or the intrabronchial injection through a bronchoscope. A gas opaque to roentgen rays would be preferable, but as none is available commercially, the oil is useful for demonstrating the lower respiratory tract. The introduction of the oil needs a careful technic and the cooperation of an experienced laryngologist. Visualization of the bronchial tree is an important aid in teaching practical anatomy. Bronchiectatic cavities are readily demonstrated. Abscess cavities, because of the swelling of the bronchial mucosa leading to the cavity, are not as easily demonstrated as they are by roentgenoscopic methods alone. Injection of cavities, easily recognized by routine roentgenology, such as are found in tuberculosis, is not to be considered as a routine proceedure.

Stulik, Chicago.

Measurement of the Hardness of Muscles in Children. Hans Opitz and H. Isbert, Jahrb. f. Kinderh. **111**:165 (Jan.) 1926.

Measurements made on children with a Mangold sclerometer gave the following results: Muscular labor carried on to the point of exhaustion produced an increase of hardness of the muscles equal to 14 per cent of the hardness during rest; in children with chronic diseases, this increase was only 10.5 per cent. This fatigue hardness disappears in from ten to fifteen minutes, sometimes in from one-half hour to one hour. Systematic exercise causes a permanent increase in hardness of the muscles which disappears only when exercise is entirely stopped. The hardness of the muscles is dependent on the extent and intensity of exercise.

MEASUREMENT OF HARDNESS OF THE MUSCLES IN CHILDREN. III. HANS OPITZ and H. ISBERT, Jahrb. f. Kinderh. **111**:177 (Jan.) 1926.

A sojourn at the seaside for children from the city causes an increased hardness of the muscles. This occurs in children who have a normal hardness as well as in those who are originally weaker or stronger. There is no direct relation between the increase in hardness and the weight curve. Therefore, sclerometry appears to be an important objective method of measuring the results of a vacation.

EHRMANN, Chicago.

VARIATIONS IN DIAMETER OF THE RED BLOOD CORPUSCLES IN CHILDHOOD. LEO PASCHERT, Ztschr. f. Kinderh. **43**:84 (Feb.) 1927.

In the twenty-two patients investigated, the average diameter of the red blood corpuscles in older infants and in children lies between 7 and 7½ microns. According to Wiechmann and Schürmeyer, this is not true for the newly born nor, in the experience of the author, for premature infants. The spreading of values is extraordinary in premature infants, much more marked than in the newly born and the large, red cells far outnumber the smaller ones. The largest value found was 9 microns. The curve of the diameters plotted against the percentage of occurrence is low and asymetrical as the result of the washing out of unripe forms into the circulation from the depots of blood formation, and is reminiscent of the curves published for pernicious anemia. In the course of childhood the spreading of values gradually diminishes, and the curve ascends sharply from a narrow base; that is, the size of the erythrocytes varies less all the time and after the third month the big cells are hardly met. The values center closely about the greatest width after the fourth month; the variation is even less marked at the end of the first year and still later is even more diminished.

The number of children investigated is too small to relate this shrinkage of values to definite periods of life. The change is gradual and occurs in children at different rates. The outstanding change, however, occurs at the end of the first three months with the disappearance of the big forms.

PAUL W. EMERSON, Boston.

Pathology, Bacteriology and Biochemistry

CONTRIBUTION TO THE PHYSIOLOGY OF GASTRIC SECRETION IN INFANCY. OTTO CORDRESS, Monatschr. f. Kinderh. **36**:150, 1927.

The author decided that the work of Rosenbaum and Hoffmann, done in 1921, should be repeated. These observers determined the amount of lactose in the stomach contents removed at frequent intervals. They found a rapid decrease with cow's milk and no great change with breast milk. They concluded that this method enabled them to determine the amount of gastric secretion.

The author has repeated much of this work, but in some respects his conclusions differ from those of the other investigators. His results show that the infant's stomach is well equipped to deliver a juice containing effective amounts of hydrochloric acid, pepsin, rennin and lipase. Such a juice is also secreted on a diet of breast milk, but breast milk does not make the demands of cow's milk. Cordress believes that acid foods temporarily spare the gastric glands, but later increase their work, due to the fact that they must constantly secrete acid over again.

The peristalsis of the nursling's stomach, while present, is not sufficient to make a good mechanical mixing of the contents.

The increase of acidity during the digestion of breast milk is due not only to the formation of fatty acids by the breast milk lipase but also to a definite acid gastric juice.

Breast milk has a p_H of from 7.2 to 7.5. It rapidly loses its carbon dioxide and so usually shows a p_H of from 6.7 to 6.85.

GERSTLEY, Chicago.

CALCIUM CONTENT OF BLOOD IN CHILDHOOD. JUN ARIMA, J. Pediat. (Tokyo), August, 1927, pp. 1126, 1133.

Studying quantitatively the amount of calcium in the serum of forty-two girls by titrating with normal solution of potassium permanganate, after converting it into calcium oxalate, the author found it to lie between the minimum of 7.3 and the maximum of 12.2 Gm. per hundred cubic centimeters, with an average of 9.97. The normal range of calcium in Japanese girls is between 8 and 11. In studying the calcium content of the blood of feeble-minded children, Arima found the range to lie between the minimum of 7.8 and the maximum of 12.0.

KATO, Los Angeles.

Nutrition

ANTISCORBUTIC VITAMIN CONTENT OF MILK OF STALL-FED COWS THROUGHOUT THE YEAR. FLORENCE L. MACLEOD, J. A. M. A. **88**:1947 (June 18) 1927.

The milk of stall-fed cows which are given a well balanced, uniform diet throughout the year will not show seasonal variation in its antiscorbutic value. Addition of a good quality of ensilage in the diet will keep the antiscorbutic potency of the milk at a high level.

IRRADIATED CHOLESTEROL. A. F. HESS, J. A. M. A. **89**:337 (July 30) 1927.

The most practical application of an irradiated food is the use of irradiated dried milk for infant feeding. This food, the specific activity of which is maintained for at least six months, prevents or cures infantile rickets and tetany. Irradiated cholesterol is antirachitic and may be used to increase the potency of cod liver oil. It has been shown that a contaminating sterol, intimately associated with cholesterol, undergoes the activation. Other sterols were irradiated and one in particular, ergosterol, which is found in yeast, was found highly effective in animals and in infants. Irradiated yeast may be employed as an antirachitic.

PREPARATION OF LACTIC ACID MILK MIXTURES FOR INFANT FEEDING. MCKIM MARRIOTT, J. A. M. A. **89**:862 (Sept. 10) 1927.

An experience of eight years with feeding several hundred infants in welfare clinics has convinced the author that there are no disadvantages to the routine and prolonged use of lactic acid milk. A single formula was used for more than 95 per cent of infants under 1 year of age, the formula consisting of whole lactic acid milk to which was added one tenth of its volume of Karo corn syrup. Later, only three fourths of the amount of lactic acid was added to the whole milk. The preparation of lactic acid milk by the addition of lactic acid to sterilized milk has been about as suitable as bacterially soured milk. The use of evaporated milk possesses some advantages. As cereals are added to the diet, the amount of sugar is reduced. The fuel value is 30 calories per ounce. All evidence seems to show that the fat soluble vitamins A and D and the B vitamin are not injured by the processes employed in evaporation of milk, but C is destroyed. Cod liver oil in one teaspoonful doses is advocated daily, especially during the winter months.

PREVENTION OF ANOREXIA IN CHILDREN. C. A. ALDRICH, J. A. M. A. **89**:928 (Sept. 17) 1927.

The author recommends early prophylaxis in combating chronic anorexia. Education of the parents in the early months of the infant's life as to what pitfalls to expect and how to avoid them was attempted in 199 consecutive cases, with the result that the group averaged 36 pounds (16.3 Kg.) above weight. No children in this group were malnourished except those suffering from physical disease.

THE SPECIFIC DYNAMIC ACTION OF FOODSTUFFS. I. ABELIN and B. KOBORI, Biochem. Ztschr. **186**:3 (June 21) 1927.

The energy obtained from foods is divided into chemical energy and heat energy. The authors feel that the form of energy acquired from food depends not so much on the type of food as on the existing intermediary metabolism. During growth, after starvation or after prolonged infectious diseases, less of the energy is given off as heat, whereas when thyroid substance is administered there is an increase in the production of heat. Experimental support was obtained by feeding meat to normal rats and to phlorizinized rats. The normal specific dynamic action of meat results in a 10 to 12 per cent increase in the metabolism. After subcutaneous injection of from 150 to 200 mg. of phlorizin, this rose to from 20 to 40 per cent. The authors suggest that the bodily requirement for carbohydrate necessitated an increase in the formation of sugar from the protein, resulting in an abnormal intermediary metabolism.

BRAHDY, New York.

CLINICAL AND EXPERIMENTAL STUDIES OF ANEMIA AND DYSTROPHIA CAUSED BY FEEDING GOAT'S MILK. E. GLANZMANN, Jahrb. f. Kinderh. **111**:1 (Jan.) 1926.

The feeding of goat's milk may lead to a dystrophic syndrome or an anemia syndrome, or to both. Dystrophia is associated with loss of appetite, distaste for goat's milk, lack of growth and loss of weight, swelling of the tongue and mouth, changes in the bones, hemorrhages into the skin and mucous surfaces and loss of resistance to infection. These symptoms clear up on an antiscorbutic diet and are closely related to scurvy. The anemic syndrome is no doubt due to a trophotoxic substance, and healing occurs only when goat's milk is entirely withdrawn from the diet. This trophotoxic substance may be fat. Bloor and Knudson have shown that red blood cells absorb fats actively from the blood plasma, and change it to a cholesterol—ester and lecithin. In cases of excessive ingestion of fat or in a poor proportion between fatty acids and cholesterin, it is understandable that a hemolysis of the red blood cells may occur. Besides this, the cause must also act on the bone marrow, for embryonic cells, megaloblasts and megalocytes and a thrombopenia are present. By using a fat-free milk and an antiscorbutic diet, one takes away the toxic substance (fat) and adds substances that stimulate the formation of blood (vitamins). Experiments in feeding were done on guinea-pigs. They were fed on vitamin-free diets. One group was given cow's milk and malt extract in addition, the other goat's milk and malt extract. Those fed on goat's milk grew more slowly but in a parallel way to those fed on cow's milk. In another series one group was given oats and cow's milk, another oats and goat's milk. Both groups developed anemia, and those fed on cow's milk had a lower hemoglobin than those on goat's milk. This is in marked contrast to clinical experience in which goat's milk causes a much more marked anemia.

ETIOLOGY OF ACUTE TOXIC GASTRO-ENTERITIS IN INFANTS. GUSTAV JORGENSEN, Jahrb. f. Kinderh. **111**:63 (Dec.) 1925.

In thirty normal stools in children under 1 year, Jorgensen was unable to isolate the Welch-Frankel bacillus *(B. welchii* or *perfringens)* according to the most modern technic of Zeiszler. Older workers have reported its presence in normal stools. Fourteen abnormal stools in children with gastro-enteritic symptoms were examined. In six of these, the Welch-Frankel bacillus was found. The cases in which it was not found were diagnosed as follows: three, parenteral infections; two, dystrophies with secondary diarrheas, and one, tuberculosis.

Jorgensen considers acute gastro-enteritis as a combination of bacterial and alimentary processes. The Welch-Frankel bacillus probably introduced into

the alimentary canal in ingested milk is only capable of producing toxins from substances containing sugar. Therefore it is advantageous to remove sugars from the diet in such cases.

IRRADIATED MILK IN THE THERAPY OF RICKETS. P. GYÖRGY, Jahrb. f. Kinderh. **111**:201 (Jan.) 1926.

György took milk mixtures suitable for each child according to age and exposed them, with frequent stirring, to the ultraviolet rays for from one-half to one hour at a distance of from 20 to 30 cm. These mixtures were fed to rachitic children in whom the extent of the rachitic process was determined by physical examination and by the roentgen ray and the serum calcium and phosphorus. No other food or medication was given, and the tests were done at a time when spontaneous healing of rickets does not occur. In sixteen out of eighteen cases, evidence of healing or improvement was found.

EHRMANN, Chicago.

REPORT OF A PATIENT WITH DIARRHEA CURED BY THE USE OF MOLL'S ALMOND MILK MIXTURE. ALEXANDER WITTENBERG, Monatschr. f. Kinderh. **36**:124, 1927.

Directions are given for the preparation of almond milk which is a casein free emulsion of almond infusion, cow's milk whey, flour and sugar. One patient was cured by this feeding. Feeding charts are given.

GERSTLEY, Chicago.

RELATION OF CONSTITUTIONAL WEAKNESS IN OSSIFICATION TO RICKETS. H. ABELS and DORA KARPLUS, Wien. klin. Wchnschr. **40**:1069 (Aug. 25) 1927.

From a review of the literature, the authors indicate that the relation of defective ossification in the new-born to subsequent rickets is in dispute. Earlier observers reported that new-born infants with soft yielding bones and gaping fontanels and sutures later developed craniotabes and other signs of rickets. Wieland, however, held that softening in the skulls of the new-born differed in location from rachitic craniotabes and usually disappeared before the latter was detectable. Occasionally the two types were coexistent ("progressive soft skull"). Abels previously reported the occurrence of a type of localized softening of the skull which he believes is due to mechanical pressure of the fetal head against the maternal pelvis, because it is found only in cephalic presentations. He admits, however, that even these infants frequently display signs of generalized defective ossification.

Abels and Karplus set aside for observation thirty-three new-born infants having hard, well ossified skulls, and twenty-five with soft cranial bones or gaping fontanels and sutures. Twenty-one (84 per cent) of the twenty-five infants who subsequently developed severe cranial rickets were from the group having soft skulls, and only four (12 per cent) were from the group having hard skulls. Slighter degrees of cranial rickets developed in approximately equal numbers from the two types. Of the twenty-six who remained free from rachitic manifestations, only one had had a soft skull at birth. Rachitic changes in the thorax and extremities were more than three times as frequent in infants who had shown soft skulls at birth as compared with those whose cranial bones had been well ossified. The average weights and lengths at birth of the infants with hard skulls exceeded those of the ones with soft skulls. There were seven infants whose cranial bones were firm but whose fontanels and sutures were gaping, indicating defective ossification of the edges of the bones only. These infants developed severe rickets.

Abels and Karplus conclude that there is a relationship between a soft skull in the new-born and later developing craniotabes and rickets. They quote the observations of others (Spietschka and Hughes) in support of this

view. They offer the concept of a constitutional inferiority of ossification as the basis for rickets. They would designate as "prerachitic ostoporosis" the neonatal manifestation of this inferiority. They admit the possibility of a true rachitic constitution or diathesis.

OLMSTED, Seattle.

EXPERIMENTAL RESEARCHES ON THE ANTIRACHITIC PRINCIPLE OF IRRADIATED FOOD. A. HOTTINGER, Ztschr. f. Kinderh. **43**:8, 1927.

It was established with the help of experiments with rats that cholesterin, olive oil, cholesterin fatty acid ester and bile salts did not show an antirachitic activity. Olive oil, the unsaponifiable fraction of olive oil, cholesterin and cholesterin fatty acid ester are susceptible to activation against rickets by irradiation with ultraviolet irradiation, but this is not true of the bile salts. The unsaponifiable fraction of cod liver oil and of the irradiated olive oil, likewise the unsaponifiable part of a solution of irradiated cholesterin in inactive olive oil, shows undiminished antirachitic characteristics. If active cholesterin preparations are allowed to stand several months, they lose their activity when they are kept in crystalline form or in mineral oil. In olive oil solution, they keep better. One cannot find an active principle in the filtrate if active cholesterin is precipitated with digitonin. If one isolates cholesterin from the precipitate, it does not show activity but it is capable of being reactivated.

If active cholesterin is heated to from 150 to 200 C. it is inactivated, but the activity can be restored. If it is heated to 100 or 120 C., biologic activity is only partly lost, and it is not lost at all if the heating is done in olive oil solution. Activated olive oil stands temperatures of from 100 to 120 C. for an hour. With olive oil as a solving agent, a stabilizing protective activity for the antirachitic principle against aging and inactivation by heat can be demonstrated. Through radiation for several hours, active olive oil and active cholesterin lose their antirachitic principle. There is a contrast between inactivation by high temperature, in which the substances can be reactivated, and the irreversible inactivation by overirradiation. The activating and inactivating influence of ultraviolet rays on cholesterin appears not to be dependent on oxidation by the quartz lamp. A purely chemical transformation product of cholesterin is not to be considered as the vehicle of activation. The natural antirachitic principle occurring in cod liver oil and the synthetic one may, by irradiation of cholesterin in vitro, show the following similar conditions: Precipitation by long standing, resistance to moderately high temperature, resistance to the process of saponification and loss of activity by intensive radiation with ultraviolet light. Dissimilar conditions are shown by precipitation with digifolin. The cod liver oil vitamin remains in the filtrate, but the active principle of irradiated cholesterin is lost.

ALIMENTARY FEVER AND INTOXICATION IN THE INFANT. H. RIETSCHEL and F. STRIECK, Ztschr. f. Kinderh. **43**:106 (Feb.) 1927.

The authors believe that alimentary fever and salt fever are in reality alike. In both an impoverishment in water is produced; this occurs in the severer form of alimentary fever, on account of vomiting and diarrhea, since in this case not only water but also mineral salts and albumin are lost to the body. This is not the case in salt fever, in which diarrhea never occurs. In severe diarrhea, great thirst and toxic conditions appear sooner. The theory that the permeability of the intestine is a result of desiccation is approved. It is clear that in such severe conditions toxic substances may finally appear, but whether the convulsions and the whole nervous symptom complex are explained by the loss of water or whether in desiccation other pathogenic and toxic factors play a part, cannot be said. The point is that the characteristic etiologic and pathogenic injury in the beginning is the loss of water. Alimentary fever is, then, the expression of a great increase in fever following a sudden deprivation of water and is a physical phenomenon. Loss of water is the principal factor in the condition of intoxication; all the rest is secondary. Finally, as

a matter of treatment, why give the child with intoxication saline solution since it leads to impoverishment in water in the tissues and that condition is already present? No adult would take saline solution to relieve his own thirst.

PAUL W. EMERSON, Boston.

INFLUENCE OF CATHARTICS AND THYROID EXTRACTS ON THE VITAMIN A DEFICIENCY DISEASE. T. SANO, J. Pediat. (Tokyo), June, 1927, p. 800.

The purpose of studying the effect of cathartics is to determine whether the artificially induced diarrhea exerts any influence on the incubation period of avitaminosis. The thyroid secretion is also thought to shorten the incubation period. Using young rats as experimental animals, the author arrived at the following conclusions: (1) If a diet devoid of vitamin A is administered to young rats, xerophthalmia appeared after an incubation period of from thirty-nine to seventy-nine days. The decrease in weight is noticeable during this period. (2) If thyroid extract is added to the same diet, the incubation period is materially shortened, producing xerophthalmia in from twenty to thirty-eight days. When the amount of thyroid is increased, the animals die before the appearance of xerophthalmia. The loss of weight is also more marked with this diet than with a diet simply devoid of vitamin A. (3) When cathartics are given frequently during the period of incubation, the prostration becomes marked and often leads to death, long before the manifestation of avitaminosis. When the diarrhea is moderate, the deficiency phenomenon appears in a normal incubation period. The loss of weight is less than with simple avitamin diet, due perhaps to a slight increase in appetite caused by slight diarrhea. (4) Roentgenologic examinations of the bones of the animals did not reveal any noticeable changes.

KATO, Los Angeles.

Prenatal Conditions

A CURIOUS CONGENITAL ANOMALY OF THE SPINE. RICHARD B. DILLIHUNT, J. A. M. A. **88**:1000 (March 26) 1927.

A boy, aged 5, presented an unusual and marked disproportion between the length of the trunk and of the extremities, due to an overgrowth of the spine. The normal number of vertebrae were present but they were greatly increased in size, especially the lower dorsal and lumbar vertebrae. The cause of this overgrowth could not be determined.

SIMPLE CONGENITAL ANORECTAL STRICTURE WITH MEGACOLON IN EARLY INFANCY. JOSEPH BRENNEMANN, J. A. M. A. **89**:662 (Aug. 27) 1927.

Congenital anorectal stricture, unaccompanied by other anomalies of that region, is apparently a rare condition; especially infrequent are reports of cases seen in early infancy or as a cause of megacolon. Six such cases are described with the marked abdominal distention, obstinate constipation and evidence of great distress, and usually vomiting. These were apparently all of the simple diaphragmatic type in which abdominal (colonic) distention was the outstanding symptom, and were promptly relieved by finger dilatation.

BONAR, Salt Lake City.

IS THERE AN EFFECTIVE ACTIVITY OF THE FETAL THYROID GLAND UNDER PHYSIOLOGIC CONDITIONS? E. MAURER, Ztschr. f. Kinderh. **43**:163 (Feb.) 1927.

The author's work is a contribution to the solution of the question of whether the thyroid of the fetus and newly born infants is active under physiologic conditions. A consideration of the known facts and the demonstration that the thyroid gland and the whole organism of the newly born

has iodine in manifest and regular distribution speak for the correctness of the view that, even in intra-uterine life, the thyroid carries on a parallel and supplementary activity of the maternal thyroid organ.

PAUL W. EMERSON, Boston.

Diseases of the New-Born

ACUTE (EPIDEMIC?) ENCEPHALITIS: REPORT OF A CASE IN A NEW-BORN TWIN, WITH HISTOLOGIC OBSERVATIONS. GEORGE B. HASSIN, Arch. Neurol. & Psychiat. **18**:44 (July) 1927.

Hassin reports a case of a twin dying at the age of 15 days. The only symptoms recognized was that of fever, which was present for two days preceding death. The child had club feet, hypospadias and congenital cystic kidneys, and the ulna and thumb were missing on the right.

The pathologic alterations in the brain were those of an acute inflammatory process. These changes were most marked in the midbrain and the basal ganglia, but were present to a lesser degree throughout. The infiltrating cells were chiefly polymorphonuclear in character, and were found in the parenchyma, perivascular spaces and within the ganglion cells, a condition exceedingly rare in acute epidemic encephalitis. However, the observations are similar to those described by DeFano in an acute case of epidemic encephalitis and also to those of experimental encephalitis. Because of these facts and the mildness of the destruction of the ganglion cells in the cord, the author concludes that this case was one of acute epidemic encephalitis.

The case is interesting from a clinical point of view. The author points out that if the child had recovered with the disease unrecognized, some sequelae such as epilepsy, mental deficiency, idiocy or behavior disorder might be expected. In other words, any of these or similar conditions observed in grown children may be caused by inflammatory lesions of the brain occurring in infancy.

AVERY, Chicago.

ERYTHEMA NEONATORUM TOXICUM (LEINER) AND GENERAL ALLERGY OF THE NEW-BORN. E. MAYERHOFER and M. KRAJNOVIĆ-LYPOLT, Wien. klin. Wchnschr. **40**:991 (Aug. 4) 1927.

In 1912, Leiner applied the term "erythema neonatorum toxicum" to a condition that was generally held to be of gastro-intestinal or "dyspeptic" origin. Mayerhofer and Kranjnović-Lypolt determined the presence of this form of toxic erythema in 46 per cent of 1,500 new-born infants examined. They contend that such frequency of occurrence speaks against any pathologic significance. Although occasionally found within a few hours after birth, the lesions usually appear suddenly on the second to the fourth day, rarely later. There are three types, a lichenoid form consisting of dark red miliary papules surrounded by a light red halo (61 per cent), an erythematous form (16 per cent), and a combination type (16 per cent). Strong infants are most frequently affected. When occurring in twins, the lesions are practically identical in appearance. They usually appear first on the face; other sites of predilection are the chest, back and elbow regions. In some cases the eruption spreads in a mild form to the extremities. The duration of the exanthem is less than two days in 46 per cent of cases, and from three to sixteen days in 54 per cent. The lesions are subject to marked and sudden changes in form, either spontaneously or as the result of inunctions of tincture of iodine, old tuberculin, placental extract, or even water (bathing). Residual lesions may be left in the form of fine scales, miliary papules, vesicles or shallow abscesses. In about 10 per cent of the cases there are faint relapses after from eight to fourteen days.

The authors believe that their investigations of toxic erythema of the newborn disprove such theories of etiology as gastro-intestinal disturbances,

retention of hematoporphyrin and difference in blood grouping of mother and child. In view of the frequency, the suddeness of onset and disappearance, the protean character and the unequal distribution, the authors believe that the exanthem is allergic, hormonic and toxic. The toxin, which is probably of maternal origin, traverses the placenta and sensitizes the fetus. In support of the allergic theory, they point out the fact that the eruption at its height is practically always accompanied by an eosinophilia. Furthermore, other allergic phenomena often accompany the exanthem, the most common of which are swelling of the mammary, thyroid and lymph glands, localized edema, vaginal hemorrhage and noninflammatory hydrocele.

CYANOSIS IN THE NEW-BORN. J. SAHLER, Wien. klin. Wchnschr. **40**:1049 (Aug. 18) 1927.

Among the commoner causes of neonatal cyanosis, Sahler names mechanical blocking of the air passages and injuries of the central nervous system. Persistent cyanosis indicates a congenital anomaly of the heart. He describes other types of transient generalized cyanosis reported in Germany. These were explained by a theory of temporary ateriovenous mixing of the blood through a patent foramen ovale as the result of disturbance in pressure equilibrium of the auricles.

The cyanosis in Sahler's patient, which was confined to the face and neck, was first observed ten minutes after birth. Ten hours later, a roentgenologic examination disclosed distinct widening of the great shadows of the vessels, both during inspiration and expiration. The cyanosis and increased shadows gradually diminished and entirely disappeared on the third day. Sahler explains the localized cyanosis as the result of pressure on the superior vena cava. Two hypotheses are advanced. Disturbance in innervation or sluggish action of the right auricle may lead to overfilling and resultant compression on the adjacent vena cava superior, or the orifice of this vessel may become partially obstructed by a projecting tuberculum intervenosum. Sahler advises roentgen-ray examination of the cardiac region and the great vessels in cases of limited cyanosis in the new-born.

OLMSTED, Seattle.

MELENA NEONATORUM ULCEROSA. RUDOLF STEINERT, Ztschr. f. Kinderh. **43**:188 (Feb.) 1927.

Twenty-four hours post partum, profuse hemorrhage occurred from the mouth and rectum of an infant, and the diagnosis was made of melena neonatorum in the hospital, where she died the day of admission. There were no ecchymotic spots on the skin, nor varices of the esophagus but by careful search near the papilla of vater an erosion the size of a pinhead was found, suggesting an ulcer, and microscopically complete destruction of the mucous membrane at this point was demonstrated. The underlying submucosa was necrotic and infiltrated and in the ulcerated tissue there was discovered a vein that was widely opened by erosion, and nearby was an artery, free but intact, the thick walls of which obviously offered stronger resistance. This ulcer of the duodenum, it must be emphasized, could not be diagnosed certainly because it was so small and until it was examined microscopically.

PAUL W. EMERSON, Boston.

Acute Infections

TREATMENT OF ACUTE INFECTIONS AND CONTAGIOUS DISEASES. J. H. MUSSER, J. A. M. A. **88**:1125 (April 9) 1927.

The author has reviewed the histories of patients admitted to the contagious disease ward of the New Orleans Charity Hospital for the last eleven months. He concludes that the results obtained with antiscarlatinal serum and with erysipelas antistreptococcic serum have been definitely and unfailingly good.

A definite, specific cure is available for the treatment in these two diseases. In meningitis, cisternal and lumbar puncture is to be preferred to simple lumbar puncture and to injection of serum through the lumbar opening. Patients with measles are much benefited by convalescent serum. For whooping cough, ether in oil given per rectum is to be preferred to ether given intramuscularly.

THE DICK TEST WITH ACTIVE AND PASSIVE IMMUNIZATION FOR SCARLET FEVER. H. D. LEES, J. A. M. A. **88**:1133 (April 9) 1927.

Fifteen of forty-eight patients with scarlet fever had negative Dick tests at the onset of the disease. A negative test does not seem to be a reliable index of immunity to the disease and cannot be relied on as an aid in the diagnosis of doubtful cases of scarlet fever. A positive Dick test was obtained in 49.8 per cent of 530 students of rural Minnesota homes with an average age of 17 years. One injection of 3,000 skin test doses of toxin, detoxified with 2 per cent sodium ricinoleate, rendered 63 per cent of the children who gave positive reactions to the Dick test negative to the reaction. Injection of convalescent serum intradermally produced an earlier and more complete blanching of the scarlet fever rash than did the concentrated Dick antitoxin. The Dick test remained positive in four of five cases following the injection of prophylactic doses of scarlet fever antitoxin.

SERUM SENSITIZATION RESULTING FROM DIPHTHERIA TOXIN-ANTITOXIN ADMINISTRATION. CHESTER A. STEWART, J. A. M. A. **88**:1220 (April 16) 1927.

Immunization against diphtheria without sensitization to serum, particularly that derived from horses, is desirable. Recent studies indicate that this end may be accomplished by the use either of anatoxin or of toxin detoxified by means of sodium ricinoleate. Until the status of these two preparations is fully established, the employment of toxin-antitoxin containing goat serum is recommended.

EPIDEMIC MENINGITIS IN THE FIRST THREE MONTHS OF LIFE. JOSEPHINE B. NEAL and HENRY W. JACKSON, J. A. M. A. **88**:1299 (April 23) 1927.

In the last sixteen years, the authors have seen fifty-four cases of meningitis in young infants, twenty-five of which have been due to the meningococcus. At this age the onset is not as acute, the fever is irregular and gastro-intestinal disturbances are common. Convulsions are not a constant feature and the classic signs of meningitis, such as rigidity of the neck and the Kernig sign, are usually absent until the case is well advanced. A bulging fontanel is nearly always found. The rash is unusual. In this series the mortality was 47.8 per cent, which was slightly higher than their mortality rate during the first year, and far in excess of that for the second year — 29.2 per cent. The sequelae were surprisingly few.

ENCEPHALITIS ASSOCIATED WITH MEASLES. JOSEPHINE B. NEAL and EMANUEL APPELBAUM, J. A. M. A. **88**:1552 (May 16) 1927.

Acute encephalitis is occasionally associated with various acute infections, especially measles, but whether this condition is related to the epidemic form it is impossible to say. Of the twelve patients studied by the authors, the mortality was 25 per cent. Of those recovering, in only one was recovery incomplete.

THE OCCURRENCE OF STAPHYLOCOCCUS AUREUS INFECTION WITH A SCARLATINIFORM RASH. FRANKLIN A. STEVENS, J. A. M. A. **88**:1957 (June 18) 1927.

Study of such a case in a 12 year old girl led the author to conclude that such cases might be distinguished by the absence of scarlatinal streptococcus, the presence of the staphylococcus and positive blanching phenomena with staphylococcus antitoxic serum.

A Case of Measles Encephalitis. F. Redlich, Ztschr. f. Kinderh. **43**:178 (Feb.) 1927.

Before the fading of the measles eruption, drowsiness developed in a child, aged 4 months, which progressed to loss of consciousness and severe but short convulsions. He showed meningeal symptoms of moderate grade on admission, myoclonic movements of the extremities, mask-like face and amaurosis of central origin; at the beginning of the second week, when the drowsiness began to diminish without relieving the amaurosis, choreic movements and general restlessness occurred. On the fifteenth day, there was a great change for the better coincident with the discharge of pus from the left ear. In three weeks more the child had recovered. Encephalitis is so rare in measles that it was observed only six times in the 5,940 cases in Boenheim's monograph. It occurs either with high temperature in the prodromal stage or with complications, especially otitis media. In the case reported here, there was an interval of fifteen days between the beginning of the nervous phenomena without fever and the discharge of pus from the ear. It is impossible to say whether this was toxic encephalitis or epidemic encephalitis.

Paul W. Emerson, Boston.

Ether Treatment of Pertussis. Akira Sato, J. Japan Soc. Infect. Dis. **1**:311 (Jan. 20) 1927.

The author states that the fundamental reason for the employment of ether in the treatment of whooping cough is still undetermined. It is for neither its bactericidal nor its anesthetic property that ether is used. From his previous reports, together with a careful review of the literature, Sato points out the following factors that influence the effectiveness of ether: (1) Ether seems more effective in older than in younger children. (2) Ether works better at the beginning of the paroxysmal stage, rather than at the onset of the disease. (3) It is more effective among the out-patients than among the hospitalized patients. (4) The presence of complications makes the treatment less effective. (5) The season of the year also influences the effectiveness. (6) The amount of food taken during treatment also has much to do with its effectiveness.

Therapeutic Effect of Artificial Sun Lamp on Erysipelas. S. Yabuki, J. Pediat. (Tokyo), August, 1927, p. 1156.

Using the sun lamp in the treatment of eight patients who had erysipelas, Yakubi concluded that the suppressive effect of the lamp on the progress of the disease is by no means absolute, but there seems to be a definite retardation in the rate of spread. The sun lamp is to be recommended for the treatment, as it decreases infiltration, at times lowers the temperature and increases the appetite. The important thing is the dosage. In general, big dosage should be preferred. The erythema of the skin is unimportant. The author prefers to employ 50 cm. distance from the beginning. In infants, a short exposure at a smaller distance is preferable to a longer exposure at a greater distance. The exposure may have to be repeated from three to four times in obstinate forms of the condition.

Kato, Los Angeles.

Chronic Infections

Pathogenic Power of B. C. G. Vaccine. Lignieres, Presse med. **35**:948 (Aug. 17) 1927.

Lignieres found that autopsies performed on animals one year after inoculation with B. C. G. tuberculin vaccine showed organisms at the point of inoculation, which resembled the tubercle bacilli but which had lost all pathogenicity.

While harmless for larger animals, B. C. G. sometimes kills the guinea-pig. For this reason, the vaccine cannot be considered as absolutely harmless. It is therefore wise to use it only in those cases in which there has been a definite history of tuberculous contact.

FRAWLEY, Fresno, Calif.

THE INFLUENCE OF BISMUTH ON THE BLOOD PICTURE OF SYPHILITIC CHILDREN. ANDREAS V. TUDOS and PAUL V. KISS, Jahrb. f. Kinderh. **111**:219 (Jan.) 1926.

The blood picture of syphilitic children is typified by polychromasia, poikilocytosis and anisocytosis. Normoblasts and monocytes are common. Injections of bismuth are followed by increase in red cells, hemoglobin and leukocytes. Normal young rats and rabbits showed a similar increase in hemoglobin and red blood cells.

THE INCEPTION OF TUBERCULOSIS (INCUBATION). BERTHOLD EPSTEIN, Jahrb. f. Kinderh. **111**:271 (Feb.) 1926.

Epstein reports eleven infants exposed continually to tuberculosis in whom a tuberculous infection developed under his eyes. These children all gave negative reactions to the tuberculin test when first seen and gave positive reactions only after repeated tests with tuberculin were made. By the incubation period is meant the time from the infection to the appearance of allergy, which Epstein found to vary between 27 and 128 days; from 3 to 7 weeks with intracutaneous or subcutaneous tests and from 4 to 10 weeks with cutaneous tests. The length of incubation has nothing to do with the prognosis. Allergy is not full-blown immediately but increases gradually. The Pirquet test becomes positive only when the titer of tuberculin has reached 1:10,000. These early reactions also disappear more quickly (in from fifteen to twenty-four hours after injection). In forty-eight hours, the whole reaction has disappeared.

ERHMANN, Chicago.

MEINICKE'S REACTION IN CHILDHOOD. PAUL DOHNAL, Ztschr. f. Kinderh. **43**:103 (Feb.) 1927.

Meinicke's reaction has great practical value over the Wassermann reaction in its possibility of being accurately performed with the smallest amounts of serum. The author's aim in this paper was to determine whether unspecific positive results occur in healthy and in sick children with enough frequency to influence the diagnosis. The specificity of this reaction in infancy and childhood was shown in 571 cases; 130 of these patients were infants. Only twice was an apparently unspecific reaction found, and in no case was even severe illness a disturbing factor in the outcome of the test. In some cases of latent syphilis in older children and in mothers, the reaction was found to be better than the Wassermann. In manifest syphilis, it was constantly positive.

COMPLETE RECOVERY FROM A TUBERCULOUS INFECTION AS DEMONSTRATED BY CLINICAL AND BIOLOGIC EXAMINATION. HERBERT KOCH, Ztschr. f. Kinderh. **43**:185 (Feb.) 1927.

A boy, aged 9, whose sister had tuberculosis of the spine and whose mother died of tuberculosis, was admitted to the hospital in 1923 with tuberculous peritonitis; he quickly improved. In 1924, he was readmitted because of a generally unfavorable condition and loss of appetite and weight, but he rapidly became better. One Pirquet test was negative, and a second one was positive. In 1925, he was admitted for the third time with impetigo and with a history of having had measles in the past year. The Pirquet reaction was negative. He was readmitted in 1926 for a sore throat, and a Pirquet reaction was twice negative as was an intracutaneous test with 0.1 mg. of old tuberculin and

and finally with 1 mg. of old tuberculin. How can one regard anergy to tuberculosis in such a case in which the patient certainly was infected with tuberculosis and subsequently recovered? In this case tuberculosis probably occurred early and healing was so complete that the patient appeared to be absolutely free from tuberculosis.

PAUL W. EMERSON, Boston.

THE DIAGNOSIS OF ACTIVE TUBERCULOSIS OF THE BRONCHIAL GLANDS AND PULMONARY TUBERCULOSIS IN CHILDREN OF SCHOOL AGE. VLADIMÍR DVORSKY, Cas. lek. cesk. **64**:1469 (Oct.) 1925.

The author discourages the frequent diagnosis of tuberculous bronchial glands in children with poor appetite, occasional low grade fever, slight increase in the shadow of the hilum or a few calcified glands and no other objective symptom except a positive Pirquet test. Engel and others feel that primary massive infections appear most frequently in infants and that active tuberculosis of the bronchial glands is rare in children between 7 and 14 years of age. A positive D'Espine sign, spinalgia from the second to the sixth thoracic segments, paravertebral or interscapular decreased resonance, anterior decreased resonance about the first rib, and a positive Pirquet reaction are not diagnostic of active tuberculosis in the glands. Two valuable signs are massive enlargement of the hilum as seen with the roentgen ray, and discordant fine râles in the region of the hilum posteriorly and in the second and third intercostal spaces near the sternum. At times, a posterior basal localized bronchitis is heard with or without a pleuritic rub. This dry rub is most often localized in the right base anteriorly and in the axilla, and is regarded as an important sign of active lesions. The pleurisy is regarded as either a collateral inflammatory reaction due to the proximity of the right mediastinal pleura or as a secondary independent pleurisy with a tendency to become exudative. Injection of graduated, increasing doses of tuberculin was of no diagnostic value. Increased sedimentation of red corpuscles was noted in all cases diagnosed as active tuberculosis of the glands. Care must be used in differentiation of inactive tuberculosis of the gland and stationary pulmonary tuberculosis. Differentiation of the severe pulmonary tuberculosis as to pneumonic, caseating, tertiary or miliary tuberculosis has little therapeutic or prognostic significance. Examination of the sputum and roentgen-ray examination are valuable in differentiating chronic bronchitis, fibrous tuberculosis, bronchiectasis, chronic pneumonia and massive tuberculosis of the glands. The history and progress together with a careful physical examination must not be neglected.

STULIK, Chicago.

Internal Diseases

ROENTGEN STUDY OF FIVE HUNDRED CHILDREN FOR THYMIC ENLARGEMENT. C. WINFIELD PERKINS, Am. J. Roentgenol. and Radium Therapy **15**:216 (March) 1926.

The association of sudden death and enlarged thymus was known 250 years ago, following the researches of Morgagni. Because an enlarged thymus may be present without any signs such as stridor, cyanosis, unconsciousness, asthma or respiratory difficulty, 500 children were studied before removal of the tonsils and adenoids. Twenty-five cases of definite thymic enlargement were found. One child, who did not show a thymic shadow, died during primary anesthesia, and at autopsy, a large thymus was found down so low that it was overlapped by the cardiac shadow. The author concludes that all children should have a clinical and roentgenologic examination for enlarged thymus. Congenital heart anomaly and enlarged thymus can be differentiated by the roentgen ray. Children under 3 years present a broad heart base which must not be confused with enlarged thymus. Roentgen irradiations are valuable in the treatment of enlarged thymus.

THE SIMILARITY OF THE ROENTGEN FINDINGS IN MULTIPLE MYELOMA AND IN SPOROTRICHOSIS. WALTER ALTSCHUL, Am. J. Roentgenol. and Radium Therapy **15**:224 (March) 1926.

Gumma and sarcoma are often differentiated in that the former usually produces a punched-out appearance and the latter has greater areas of destruction of bone. In the case reported, the roentgenograms were identical with those described as multiple myeloma; that is, with multiple areas of rarefaction, circular or oval in shape and varying in size so that the entire bone looks as if it had been chewed out by a tumor mass. On study of the material removed the condition was found to be sporotrichosis, caused by the spore forming, filamentous fungus, *Sporotrichum*.

STULIK, Chicago.

GIARDIASIS IN MAN: ITS PREVALENCE AND RELATION TO DIARRHEA AND TO GALLBLADDER DISEASE. WILLIAM C. BOECK, Arch. Int. Med. **39**:134 (Jan.) 1927.

Different species of *Giardia* have been found parasitic in man, dogs, cats, rabbits, rats, mice and frogs, and while they vary from each other chiefly in their size and shape, they all have certain morphologic features in common. A detailed description is given of *Giardia lamblia*. All species of *Giardia* live in the small intestine (duodenum and jejunum) of their host. *Giardia* has no known forcible means of invading the tissue, and it is never found deep in the mucosa of the properly fixed tissues.

The author believes that more children are infected than adults and bases his conclusion on an analysis of a table which summarizes some of the numerous protozoan surveys completed during and after the World War by European and American protozoologists. He cites infants as young as 3, while the others were 3, 9, 11 and 12 months (two), respectively.

The incidence of infection varies with environment and sanitation.

The author discredits the part played by rodents and believes it is likely that unhygienic conditions, and uncleanliness on the part of parents and others in the family who handle the infant or child, are instrumental in spreading the infection to the infant.

As yet no efficient method of treatment has been discovered.

Protozoologists and physicians are divided in their opinion in regard to the question of the pathogenicity of *Giardia lamblia* in man. His own opinions are based on isolated cases for evidence of proof or on statistical studies of protozoan surveys covering hundreds of cases. Statistically, *Giardia* does not appear to be the cause of children's diarrhea.

"A general criticism that seems to apply to all claims that *Giardia* is pathogenic and causes diarrhea, symptoms of abdominal pain, tenderness, nausea and vomiting is that, clinically, no characteristic symptomatic onset has been described that would suggest the beginning of the infection or the pathologic process, should the latter not coincide with the date of infection."

In the relationship of *Giardia* to disease of the biliary tract, one case is cited in an adult, in which *Giardia lamblia* was demonstrated in the gallbladder following its removal.

Boeck cites as a matter of interest the history of the illness of a boy, aged 4, who showed true disease of the biliary tract as demonstrated by operation and improvement of symptoms, though the *Giardia* infection has persisted since operation, and no *Giardia* were found in the gallbladder on its removal. There is no evidence of scientific value at present to support the theory that *Giardia lamblia* is concerned in the etiology of arthritis deformans, certain forms of neurasthenia, melancholia with loss of weight and such symptoms as nausea, vomiting, belching of gas and epigastric pain and tenderness.

THE RED CELL COUNT IN ARTHRITIS. E. G. PIERCE and RALPH PEMBERTON, Arch. Int. Med. **39**:421 (March) 1927.

Pierce and Pemberton present a detailed discussion of the technic of collecting blood for the red cell count, with the advantage of their method stressed, as against the usual procedure described in textbooks.

The study shows a comparison of the first drop of blood drawn with the succeeding drop in normal persons, and persons suffering from mild and severe arthritis. The results are interesting and demonstrate a difference "in the number of red cells per cubic millimeter of blood first issuing from a stab of the finger in the patient with arthritis as compared with later issuing blood, in that the count made from the first blood tends to give lower figures. While this difference also obtains among normal persons and among patients with mild arthritis, it does so with less frequency. This observation is interpreted as indicating altered circulatory conditions in arthritis, probably in the nature of vasoconstriction, and is in line with other evidence to the same end. It is also evident that, even in normal persons, the drop of blood first appearing, especially if the stab is shallow, does not necessarily yield a blood count representative of the general circulation and should be discarded."

"It is also of interest to note," the authors say, "that in some observations by the present authors, the effect of exercise and the drinking of coffee has been to increase in a few moments the count of the first drop; and, in the case of coffee, to change the minus first to a plus first drop."

The work of the authors is given graphically in five tables.

THE RED CELL COUNT IN ARTHRITIS. CAROLINE Y. CROUTER and F. A. CAJORI, Arch. Int. Med. **39**:429 (March) 1927.

Because the work on this subject by Pierce and Pemberton suggested the existence of an abnormal peripheral circulatory condition in these patients, the present author undertook this study in the hope of checking up the work by entirely independent means, and attacked the problem in various ways. Differences in the red cell content of specimens of blood would be accompanied by differences in certain of the physical and other properties of the blood. For this reason the first and freely flowing drops were compared as to specific gravity, total solids, relative viscosity, iron content and intensity of spectral bands.

The technic for collecting the specimens of blood, developed and described in the previous article, was followed scrupulously, and corroborates the observations of Pierce and Pemberton. The authors state: "The conclusions of Pierce and Pemberton are in general confirmed in the present series. In normal persons the red cell count of the first drop of finger blood was frequently (43 per cent) higher than the count of the freely flowing blood. The majority of patients with arthritis showed the opposite condition and had a lower count in the first drop of finger blood than in the freely flowing blood."

SPLEENS FROM GAUCHER'S DISEASE AND LIPOID-HISTIOCYTOSIS: THE CHEMICAL ANALYSIS. WILLIAM BLOOM and RUTH KERN, Arch. Int. Med. **39**:456 (March) 1927.

The clinical and anatomic differences between these two diseases, particularly by one of the present co-authors (Bloom), have previously been described; therefore, the authors state that their purpose in this article is to report the striking differences in the chemical analyses of spleens from these two diseases.

A brief discussion of microchemical analysis is given with a résumé of the work on chemical analysis previously done by others, and a comprehensive account of the authors' own material and method is given. The material used consisted of a portion of spleen fixed in solution of formaldehyde from a patient with Gaucher's disease; fresh portions and portions fixed in solution of formaldehyde from the spleen of a patient who had had Niemann's disease, and a fresh portion of a slightly enlarged red spleen from a young adult with bronchopneumonia. The material from the latter was obtained at necropsy, while the other two spleens were removed at operation and fixed immediately.

The results of the various determinations are summarized in three detailed tables. The authors conclude that a few cases of a form of large cell splenomegaly, for which the name lipoid-histiocytosis is proposed, have in the past been erroneously reported as examples of Gaucher's disease. Reports of the anatomic differences between the two conditions have been published previously.

The microchemical reactions of the material present in the large cells in lipoid-histiocytosis (Niemann's disease) indicate that this material is lipoid in character and probably belongs to the phosphatid group.

In Gaucher's disease, the large cells do not give any of the lipoid reactions in a typical manner. They usually give the reaction for iron.

Chemical analyses prove the spleen in Niemann's disease to contain less total nitrogen than the spleen in Gaucher's disease or the normal spleen, but a decidedly increased amount of phosphorus. The total ether and alcohol soluble extractives are also greatly increased in Niemann's disease.

The stored material in lipoid-histiocytosis is chiefly phosphatids, probably lecithin, and cholesterol. In Gaucher's disease the material is chiefly kerasin.

CONGENITAL VENTRICULAR SEPTAL DEFECT IN A MAN, AGED SEVENTY-NINE. EDWARD WEISS, Arch. Int. Med. **39**:705 (May) 1927.

"Ventricular septal defects," says the author "are usually situated just beneath the aortic cusps, anterior to the undefended space, and are frequently associated with other anomalies. Rarely do they occur alone. The following case is unique in the location and large size of a congenital ventricular septal defect unassociated with other anomalies. The age of the patient and the absence of cardiac symptoms other than a terminal cyanosis are additional features of interest."

The author cites a complete report of the case, giving the following salient points in physical examination:

An aged white man, with marked cyanosis of the hands and feet, showed some engorgement of the veins of the neck; the examination of the heart revealed an intense systolic thrill, at the ensiform cartilage and a loud, harsh systolic murmur. The murmur could be heard all over the cardia, but was loudest at the ensiform cartilage. The aortic and pulmonic second sounds were not accentuated. It was difficult to outline the heart borders, but there did not seem to be an enlargement either to the right or to the left. Examination of the abdomen showed the liver edge palpable two fingerbreadths below the costal margin, but it was not tender. The spleen was not palpable; evidence of ascites was not found.

"From the electrocardiogram, taken two days after admission, there was evidence of right ventricular preponderance and myocardial degeneration."

At autopsy, the striking feature of the heart was the large defect of the interventricular septum situated in the posterior half of the septum, about midway between the apex of the left ventricle and the mitral ring. The location of the defect, its large size, the smooth, fibrous edge, the aneurysmal communication with the right ventricle and the natural openings between the muscle columns near the apex of the right ventricle were features that distinguished this as a congenital lesion.

"All through life the defect did not interfere in any way with good cardiac function; the shunt of blood was probably from the left to the right. During the last days of life it is probable that a reversal of the shunt occurred sufficient to produce cyanosis.

"The diagnosis of cardiac defects belonging to this so-called non-cyanotic group usually does not offer any great difficulty. The presence of striking physical signs and the absence of cardiac symptoms are characteristic features A peculiar harsh murmur of unusual rhythm and intensity, often accompanied by a thrill, situated to the left of the sternum in the first or second interspace, or over the middle of the precordium, and in many instances associated with evidences of dilatation of the pulmonary artery, are the most important diag-

nostic features of this noncyanotic group. Such physical signs in a person without a history of rheumatic fever or other illnesses commonly causing endocarditis, readily permit a diagnosis of a congenital defect belonging to this group."

Perhaps the most interesting feature of this case report is the rarity of the type of defect.

LOEBER, New Orleans.

DIAGNOSIS AND TREATMENT IN PYLORIC STENOSIS. E. LESNE and M. COFFIN, Nourrisson **14**:329 (Nov.) 1926.

The authors consider their subject under the two commonly recognized forms: (1) pyloric stenosis, in which a definite pyloric tumor is present, and (2) pylorospasm.

In the case of stenosis, they minimize the value of peristaltic waves and a palpable tumor and stress the importance of the information gained through gastric lavage and roentgen-ray examinations. When a true organic stenosis is present, early surgical relief is urged. Acute and chronic forms of muscular hypertrophy are described.

In the cases of pure spasm, one can demonstrate the absence of complete stenosis by the passage of the stomach tube and also by roentgen-ray examination. Under the fluoroscope, the contractions are of shorter duration and are less intense than in the organic types. In the cases of spasm, the course may be protracted but the ultimate outlook is good. A few exceptions are cited; for example, one case reported by Grulee and Lewis. In the medical treatment of pylorospasm, the importance of antispasmodic drugs is recognized. In cases associated with tetany, calcium chloride in large doses and ultraviolet radiations meet the indications.

The article is a comprehensive review of the subject, but offers little that is new to those familiar with the American literature.

THE ANEMIAS OF INFANCY. LESNE and LANGLE, Nourrisson **15**:65 (March) 1927.

The fact that any severe illness or nutritional disturbance in an infant is accompanied by a change in the blood picture makes a satisfactory classification of the anemias of infancy particularly difficult. The authors describe four varieties:

1. Simple anemia, including the rare form of congenital anemia which has been given considerable space in American journals in recent years.

2. The chlorotic type of anemia due to a definite iron deficiency and characterized by a low color index.

3. The pseudoleukemic or von Jaksch type of anemia. This is the most severe and the most serious type and has a high mortality. The blood picture shows a marked leukocytosis of from 20,000 up to 125,000. Myelocytes are common, and clinically one finds an enlarged liver and spleen.

4. Pernicious anemia, which is uncommon.

Important causes of these anemias are: syphilis, digestive disorders, rickets, tuberculosis and various infections and intoxications.

The usual forms of treatment are outlined. The advisability of splenectomy in infants is decried. The value of transfussions is emphasized, and finally mention is made of the use of actinotherapy and irradiation with the ultraviolet rays.

CONGENITAL HEART DISEASE. S. CORDEY, Nourrisson **15**:147 (May) 1927.

In the case that Cordey describes, a clinical diagnosis was made of patent interventricular septum with probable stenosis of the pulmonary artery. A distinct systolic murmur was audible all over the precordium but was heard

best in the left third intercostal space and transmitted to the back. There was also some cyanosis of the lips. The necropsy, however, did not show any congenital cardiac defects or valvular lesions, though the heart was large and the wall of the right ventricle was thickened. The author advances various hypotheses to explain the thickened myocardium but finds none entirely satisfactory. He believes, however, that the increased force with which the blood was expelled from the right ventricle into the pulmonary artery could explain the presence of the systolic murmur.

McCLELLAND, Cleveland.

THE BLOOD PICTURE AND DIGESTIVE LEUKOCYTOSIS IN VARIOUS CONSTITUTIONAL ANOMALIES. H. F. TUR, Jahrb. f. Kinderh. **111**:49 (Dec.) 1925.

Tur studied sixty-nine children whom he divided into four classes. The following represents the blood picture with the stomach empty:

1. Normal children had from 75 to 90 per cent hemoglobin; from 4,190,000 to 5,200,000 red cells; from 0.8 to 0.9 hemoglogbin index and from 6,600 to 11,350 leukocytes. The leukocyte formula in all twenty cases was: neutrophils, 51.6 per cent; small lymphocytes, 35 per cent; large lymphocytes, 2.7 per cent; monocytes, 7.9 per cent; eosinophils, 2.7 per cent; basophils, 0.7 per cent.

2. Asthenic children had between 68 and 85 per cent hemoglobin; from 3,800,000 to 5,060,000 red cells; from 0.7 to 0.9 hemoglobin index, and from 6,200 to 11,093 leukocytes with a moderate lymphocytosis (40 per cent).

3. Lymphaticohypoplastic children have a blood picture similar to the asthenic children with from 68 to 80 per cent hemoglobin; from 3,960,000 to 5,060,000 red cells; from 0.8 to 1 hemoglobin index, and a lymphocytosis averaging 45 per cent.

4. Neuro-arthritic children, of which there were only nine, had from 75 to 95 per cent hemoglobin; from 4,500,000 to 5,000,000 red cells; from 0.8 to 0.9 hemoglobin index and an increased leukocytosis (average 9,000), of which 43 per cent were lymphocytes. Thus, these cases showed more lymphocytes than the asthenic children but less than in the lymphaticohypoplastic children.

In all four classes, the leukocytosis increased with the age of the child.

Following a diet of 300 Gm. of milk, two eggs and from 60 to 80 Gm. of bread, the following changes were noted: After one hour, leukopenia occurred in normal children; this was followed in three hours by a leukocytosis of from 15 to 45 per cent. After one hour, lymphocytosis occurred in lymphaticoasthenic children and was followed in three hours by a leukocytosis of 7 to 34 per cent. After one hour, in children, a slight leukocytosis occurred in thirteen of twenty asthenic children and in three hours in nineteen of twenty asthenic children. After one hour in arthritic children, a leukocytosis occurred that was followed in three hours by a leukocytosis that was even more marked than when the stomach was empty.

INTESTINAL INFANTILISM. OSKAR GODTCHE, Jahrb. f. Kinderh. **111**:80 (Dec.) 1925.

Godtche considers dysentery an exciting cause of intestinal infantilism which leads to decreased resorptive ability of the injured gastro-intestinal tract. The child's constitution and hunger cures probably increase the failure of resorption.

GASTRECTASIA IN CHILDREN. BOGEN and SCHIEMANN, Jahrb. f. Kinderh. **111**:94 (Dec.) 1925.

Gastrectasia is a condition that has been neglected during the last ten years. It occurs as a functional disturbance due to a diet faulty in both quality and quantity, which eventually leads to an enlargement of the stomach manifested by the low position of its greater curvature.

In 200 normal children, the lower curvature of the stomach was 2 or 3 cm. below the umbilicus when the stomach was distended with gas and from 3 to 5 cm. below when the stomach was distended to a maximum. In cases of gastrectasia the lower margin was 1 cm. above the umbilicus in one fourth of the cases, in one fourth at the umbilicus and in the rest from 1 to 4 cm. below the umbilicus.

Symptoms associated with gastrectasia are loss of appetite, loss of weight, pallor, often headaches, abdominal pain soon after eating and in older children, pressure and a feeling of fulness. The emptying time of the stomach was always more than five hours. In the cases in which gastric analysis could be made, there was usually a reduction in free hydrochloric acid. Therapy consisted in a diet of five meals daily, given regularly and punctually in the form of purées and liquids as much as possible. Carbohydrates were given in large quantities because of their shorter stay in the stomach; sweets, however, were interdicted. Fats and proteins were reduced. To accomplish this, milk was skimmed. Raw fruit was interdicted at first and later was cautiously added. Improvement followed in two or three weeks, and the stomach usually resumed its normal size in from one to three months.

THE USE OF PANCREAS IN THE TREATMENT OF GASTRO-ENTERITIS. PHILIPP LEITNER, Jahrb. f. Kinderh. **111**:105 (Dec. 25) 1925.

Leitner has used tablets of pancreas in cases of colitis, dysentery and enteritis, intoxication and decomposition with good results. This is a preliminary report.

EHRMANN, Chicago.

PERIODICAL PATHOTHERMIE. HERMANN VOLLMER, Ztschr. f. Kinderh. **43**:88 (Feb.) 1927.

A boy who had been born two weeks prematurely and whose parents and one sister were neuropathic, suddenly became blue at the age of 5 weeks; he became blue twice thereafter in the following weeks and seemed weak and distressed for half an hour. He perspired profusely and breathed with difficulty, his respirations being slow, painful, jerking and accompanied by retraction of the epigastrium. He was under observation from the age of 8 weeks to 16 months, and in addition to being underweight (at 16 months his weight corresponded to that of an infant 5 or 6 months old) and underheight, his length corresponding to that of an infant aged 10 months, he showed paroxysmal sweating, extreme lability of temperature which increased with his age and finally periodic hyperpyrexia with simultaneous disturbances of the water economy, great loss of appetite and some acrocyanosis. Especially interesting is the sudden and great variation in weight, amounting to 100 Gm. in a day, associated with variations in temperature but without diarrhea. The temperature was normal up to the age of 3 months, when the infant had otitis media and bronchitis. At 11 months he began to have regular rises in temperature, which in a few days reached 107 F., with losses in weight during this time amounting to 700 Gm. The weight curve was a mirror picture of the temperature curve, and the two-fold variations occurred at intervals of four weeks.

The periodicity pointed less to a morphologic cause than to a disturbance of function. The loss of weight that regularly accompanied the rise in temperature could be due only to a disturbance of the heat-regulating mechanism. The hypophysis plays a dominating rôle in water economy, especially that part which lies nearest the tuber cinereum. An assumed periodic disturbance of the function of the hypophysis would best explain the simultaneous disturbances of temperature and weight. The steplike development of the child would thus be brought in harmony with the picture and also the many appearances of a disturbed vegetative nervous system, since this system is so closely associated with the endocrine system.

STUDIES IN MYXOEDEMA: SEVENTH COMMUNICATION. ANOTHER YEAR OF INDIVIDUAL DOSAGE OF THYROID EXTRACT IN CHILDREN AND YOUNG ADULTS WITH HYPOTHYROIDISM. WERNER KORNFELD and EDMUND NOBEL, Ztschr. f. Kinderh. **43**:65 (Feb.) 1927.

The regulation of the dose of thyroid extract according to the square of the sitting height has been entirely satisfactory for more than two years so far as improvement in appearance and static motor function go, but a higher dosage appears necessary to overcome the mental retardation.

THE LEUKOCYTE PICTURE IN TRUE PNEUMONIA IN CHILHOOD. ERNST STETTNER, Ztschr. f. Kinderh. **43**:122 (Feb.) 1927.

A certain picture exists in the condition of the blood in the regular course of true pneumonia. If the patient recovers, for two days a series of pictures occurs in the blood; a quickly rising and quickly falling neutrophilia; leukocytes with undivided nuclei gradually increasing as a strong means of defense, and leukocytes with divided nuclei gradually returning to a majority, accompanied by unripe cells, as an expression of elective migration to the focus of disease and a transient exhaustion of the marrow. In the beginning there is a lymphopenia, after defervescence a lymphocytosis. Both phases are accompanied by an increased washing out of young lymphocytes. In the transition from one stage to the other there occurs a lymphatic crisis in the form of a temporary increased complement of ripe cells containing azure granules and displaying a bright blue cell body. This, in general, is the picture, but it is modified by a great number of factors.

PEPTIC ULCER OF THE ESOPHAGUS WITH RUPTURE INTO THE LEFT PLEURAL CAVITY. S. ROSZAK, Ztschr. f. Kinderh. **43**:181 (Feb.) 1927.

Primary ulcers of the stomach and duodenum are rare in childhood and one has never been previously reported before the fifth year, though secondary ulcers are often described. In 1,147 autopsies of children between 1 and 10 years, only nine instances of chronic round ulcers were found. A child, aged 2 years, suddenly became ill with fever and headache and vomited once. Pneumonia was found on the fourth day; the crisis occurred on the thirteenth day, and a typical empyema was discovered on the nineteenth day. The stools that previously had been normal became tarry. The vomitus contained dark masses, and by puncture the same sort of material was obtained from the left side of the chest. Death occurred on the twenty-third day. Besides pleurisy with purulent effusion and fibrinous pericarditis, autopsy showed dilatation of the lower part of the esophagus with a pea-sized oval ulcer on the surface toward the left lung, in communication with the left pleural cavity. The ulcer was of long standing and of unknown origin.

PAUL W. EMERSON, Boston.

Nervous Diseases

THE ETIOLOGY OF INFANTILE ACQUIRED HEMIPLEGIAS. E. R. FORD and A. J. SCHAFFER, Arch. Neurol. & Psychiat. **18**:323 (Sept.) 1927.

The authors review the literature as to the cause of hemiplegias in infants, excluding the cases due to heart disease, congenital defects of the brain, postnatal traumatic palsies, meningitis and abscesses. They also studied the histories of forty-three similar cases from the Harriet Lane Home.

The acute hemiplegias of children usually occur under the age of 6, either without discoverable antecedent, or during the course of some febrile disease, frequently during the convalescence. The cases associated with acute infectious

diseases are due to vascular lesions. Those which occur early in the course of the illness are usually the result of invasion of the blood stream by the primary organism, or that of a secondary infection. The palsies that develop during the convalescence are the result of vascular lesions of the cerebral vessels, as described by Wiesel and others. Concerning the cause of hemiplegias occurring in apparently healthy children, they are unable to reach any final conclusions. Anatomic evidence was not sufficient to show that they were encephalitic in origin. In the few acute cases studied of this group, the lesions are vascular in character and similar to those of the acute infectious type.

The authors point out that many other diseases of the central nervous system occurring in childhood have the same relation to the acute infectious diseases as do the hemiplegias.

AVERY, Chicago.

FOCI OF INFECTION IN CEREBROSPINAL MENINGITIS. A. B. MARFAN, Nourrisson **133**:15 (May) 1927.

If the foci of infection in cerebrospinal meningitis are so located as to produce blockage in the circulation of the cerebrospinal fluid, these cases present serious difficulties in diagnosis and treatment. It is necessary to locate the points of obstruction and to deliver the specific serum directly to them. In infants with an open fontanel, it is often easy to prove ventricular involvement by puncturing through the fontanel and of course, if cloudy fluid is obtained, serum can be introduced at the same time. Cisternal puncture will reveal the presence of exudate at the base. Explorations can also be carried out at different levels of the cord and in the subarachnoid space over the cerebral hemispheres. It must be remembered that all these procedures are hazardous. Attention is drawn to the suggestion of Blackfan of introducing air into the subarachnoid space of the cord and then studying the distribution of the air afterward by means of roentgenograms. Marfan also advocates the employment of autogenous vaccines in those cases that do not respond promptly to the antimeningococcic serum.

MCCLELLAND, Cleveland.

PATHOGENESIS AND THERAPY OF MONGOLIAN IDIOCY. JENS VAS, Jahrb. f. Kinderh. **111**:4 (Dec.) 1925.

In eight cases of mongolian idiocy, the Loewy reaction was negative in 100 per cent. There was no mydriasis after injection of a few drops of epinephrine into the conjunctival sac; consequently, no sympathaticotonias. The Aschner reflex was positive in 100 per cent of the cases, i. e., there was a retardation of the pulse when pressure was made on the bulb — consequently, a vagotonus. The Sergent line appeared in 75 per cent of the cases (this is a white line that appears when the skin is scratched with a sharp instrument in suprarenal insufficiency due to a failure of the peripheral circulation to fill with blood). The blood pressure was less than normal in from 55 to 65 per cent of the cases. The blood clotting time was increased. The last two conditions indicate a reduction in the suprarenal hormone.

The literature and a few of the author's own cases have shown that the following pathologic processes are present in this condition: a smaller brain than normal, flattening of the gyri, inflammatory reactions of the meninges, sclerosis of the surface of the brain, thickened neuroglia, sclerotic corpus callosum, enlarged hypophysis, small sclerotic thyroid, failure of development of the cortex cells of the suprarenals and increased connective tissue of the thymus.

Some of the patients showed slight improvement following the administration of a mixture of thyroid, testis, suprarenal and hypophysis for males and thyroid, ovary, suprarenal and hypophysis for females.

A Case of Porencephaly. H. Kikuth, Jahrb. f. Kinderh. **111**:114 (Dec.) 1925.

A case of porencephaly is reported in a child who died at the age of 13 months. At autopsy, a large defect of the right hemisphere of the cerebrum was found. The symptoms resembled those of lethargic encephalitis with convulsions, rigidity, somnoience and nystagmus, and a masklike appearance of the face. The history suggests an injury at birth as the probable cause of the condition.

Determination of Intelligence in a Young Child. Justus Schlesinger, Jahrb. f. Kinderh. **111**:195 (Jan.) 1926.

There is an important criterion for judging the mental develoment of a child in the contrast between its playful imagination and reality. Too little or absolute lack of development of this faculty suggests mental deficiency.

The Facialis Phenomenon. Julius Hargardler, Jahr. f. Kinderh. **111**:225 (Jan.) 1926.

Hargardler examined 131 children over 2 years of age with the facialis phenomenon. One hundred and nineteen of these were definitely neuropathic. Several of these showed mild forms of tetany for they had headache, migraine, spasms of the stomach and bowls and acroparesthesias which disappeared when cod liver oil was given. In none of these was Erb's phenomenon found at the first visit, but it was found in some on repeated testing; that is, the cathodol opening contraction was less than 5 milliamperes and the anodal opening contraction was less than 3.5 milliamperes.

Hargardler reported twenty-four cases showing a positive Chvostek's sign, in eleven of which the sign disappeared when the cheek was rubbed or heated, thereby producing a hyperemia. He considers that the condition in neuropaths at least is due to a spasm of the blood vessels which disappears temporarily when hyperemia is produced.

Ehrmann, Chicago.

An Unusual Case of Congenital Muscle Weakness. Hans Temming, Monatschr. f. Kinderh. **36**:130, 1927.

Temming reports a child, aged 8 months, with congenital weakness of the entire muscular system. The disease was differentiated from myotonia congenita by the normal reflexes and the normal electrical excitability. The author believes it to be a hitherto undescribed condition.

"Lightning Convulsions." Heinrich Lehmkuhl, Monatschr. f. Kinderh. **36**: 138, 1927.

By "lightning convulsions," Moro and later Lederer described convulsions occurring in infants, aged from 4 to 6 months, characterized by lightning like spasms. The head is bent forward, the shoulders shrugged and the legs drawn to the body. The process is repeated frequently. The convulsions are probably related to petit mal. The author reports two cases which were interesting in that one seemed to follow a slight infection.

Gerstley, Chicago.

The Nature of Psychic Infantilism in Childhood. Gött, Ztschr. f. Kinderh. **43**:1 (Feb.) 1927.

Two cases of psychic infantilism are described and discussed.

Case 1.—A boy, aged 6, showed the body development of a child aged from 1 to 1½ years, and while he could not speak he was interested in his surroundings, was a good mimic, showed a preference for different physicians and nurses and was sensitive about his size and inability to speak.

CASE 2.—A boy, aged 6, who was 7 cm. under the normal height, had developed slowly from the beginning, showed some signs of cretinism, narrow lid spaces with epicanthus, open mouth, pawlike hands with short, plump fingers and a good reaction to thyroid treatment; he was slender and had soft, thick hair and a moist skin, and stood with marked lordosis. He could speak a little but the speech was indistinct, and though he was by no means dull he seemed to be too lively, too excitable and too curious.

It is difficult to classify such patients whose personality has not reached the level of 7 or 8 years of age, when psychic infantilism begins, by which is meant a standing still of the personality of the child, who reaches this age well rounded out but who cannot go further. There may or may not be retarded body growth. Such proportional development is not characteristic of imbecility. These children show good power of attention, begin to speak at the proper time, can be mildly educated, busy themselves sensibly within their limits and do not present the lack of understanding such as goes with feeblemindedness. It is best, however, to think of psychic infantilism as not different in nature from feeblemindedness, as all causes producing one may produce the other, including disturbance of the endocrine secretions.

CEREBELLAR ATAXIA AND PSYCHIC BLINDNESS AFTER INJURY IN A CHILD, AGED TWENTY-ONE MONTHS. F. REDLICH, Ztschr. f. Kinderh. **43**:175 (Feb.) 1927.

An infant fell in a vessel containing lye and drank some of it two weeks before admission to the hospital. Two hours later, he became cyanotic and could hardly breathe, and after artificial respiration was given and the stomach was washed out he had a slight convulsion. He was unconscious for four days and the temperature went up to 104 F., gradually coming down to normal four days before entrance. For a week the parents noticed that the child did not recognize objects placed before him and that he could neither sit nor stand. Neurologically, he could not fixate and gave the impression of being blind, but there were no changes in the eyegrounds. With help he could walk in an ataxic manner, and when he attempted to sit up he fell to the right. Without support, his head fell backward. His reflexes were lively, and there was resistance to passive movements. Lumbar puncture was negative save for increased pressure. The Pirquet test was ++. After a month, he was able to see, but he did not know what he saw (psychic blindness). By the end of another month, he had entirely recovered. The diagnosis was trauma to the occipital lobes of the brain and to the cerebellum, probably a hemorrhage.

PAUL W. EMERSON, Boston.

Diseases of the Ear, Nose and Throat

NASOPHARYNGEAL ATRESIA. JOHN EDMUND MACKENTY, Arch. Otolaryng. **6**:1 (July) 1927.

The etiology of nasopharyngeal atresia is both congenital and acquired. Often intra-uterine pathologic alteration causes atresia, which is mistaken for the true congenital form. In the order of frequency acquired, atresia is caused by: syphilis, trauma (often following tonsillectomy), diphtheria, tuberculosis and simple inflammation. The symptoms are: partial or complete stoppage of nasal breathing, changes in the nasal mucosa due to lack of aeration and stagnation of secretions, and a deafness, which varies from slight to 75 per cent or more loss of hearing. Occasionally, bronchitis is seen. Diagnosis is made by direct examination, but the condition must not be confused with neoplasms. Prognosis depends on the extent of the atresia, its cause and the method of treatment. Treatment as given by the author consists of two procedures. The principle of each is so to cover the posterior surface of the soft palate that adhesions cannot form, as this and contraction of the scar tissue are the most frequent causes of operative failure. In his first

procedure, two flaps of tissue are made by dissecting off the lower and anterior surface of the obstructing membrane, then cutting it through at the posterior and lower limit of the nasal space. The flaps so made are drawn upward and backward and sutured to the posterior surface of the soft palate. In the second method, to be used when there is little tissue for plastic purposes, the soft palate is split by a vertical incision with a horizontal incision crossing this at its lower limit. The mucous membranes above and below are sutured over the muscle edges to prevent adhesions. Retraction of the cut muscles permits a good opening. Seven of ten cases were successfully treated by the first and the remaining three by the second method.

Bronchiectasis Associated with Disease of the Nasal Accessory Sinuses. Louis H. Clerf, Arch. Otolaryng. **6**:28 (July) 1927.

Judging from the study of many clinical cases and experimental work, it is probable that chronic nasal accessory sinusitis is responsible for a large number of the cases of bronchiectasis observed, due to direct inhalation of infective material. Bronchiectasis is also caused, especially in children, by peribronchitis associated with peritracheobronchial adenitis resulting from acute infectious diseases that involve the lungs. As nasal sinusitis has such a marked effect on chronic bronchitis, it is to be expected that it also has a great influence in causing bronchiectasis. Any condition of chronic cough deserves a careful bronchoscopic examination and an examination of the sinuses. Treatment for bronchiectasis is not complete until the patient received proper care for any existing sinusitis.

Deafness in School Children. Edmund P. Fowler, Arch. Otolaryng. **6**:43 (July) 1927.

One thousand children in one of the better New York City schools were tested in groups with the phonograph-audiometer (4A). Those with a loss of hearing of 9 sensation units or less were tested individually with the 2A audiometer and were given the usual examinations of the ear, nose and throat. A questionnaire was answered by each pupil, giving data relative to diseases of the ears. Classification was then made into three groups, each with three subgroups, according to the symptoms. Otitis, present or past, was found in a large number of cases. The author feels that before these types can be definitely used in determining types of deafness or in estimating the future loss of hearing, a great deal more work must be done.

Barnett, Chicago.

Orbital Inflammations in Early Childhood. Saeger, Klin. Monatsbl. f. Augenh. **78**:650 (Aug.) 1927.

Since one of the commonest causes of orbital inflammation in the adult is some organism of the accessory nasal sinuses, the author reviews the development of these sinuses in the infant according to the observations of Onodi, Zukerkandl and others. He reviews cases of orbital cellulitis arising from the accessory sinuses in early childhood. One occurred in an infant, aged 5½ months, the infection arising in the frontal and sphenoid sinuses; another in an infant, aged 7 months, began in the antrums. Telepner reported an infant, aged 1 year, who had had an infected antrum which caused orbital cellulitis, thrombosis of the cavernous sinus and death. In one of the author's patients from the Freiburg clinic, a boy, aged 3, sphenoiditis was present. Marked cellulitis with exophthalmos developed during an attack of whooping cough. The orbit was explored, the bony wall of the ethmoid found involved and the ethmoid cells were opened and curetted. A pneumococcus was the infecting organism. In a second case, no nasal origin could be found for the infection. The patient was an infant, aged 19 weeks, who had left exophthalmos. The orbit was incised and the evacuated pus showed *Staphylococcus aureus;* however,

disease of the bony walls was not found, and the sinuses were apparently normal. There was apparently no possibility of infection from the skin, so that a metastatic origin was considered probable. In a girl aged 2½ years, who had pneumonia following measles, the origin of the cellulitis was a left purulent otitis media. Postmortem examination showed a thrombosis of the left venous sinus and bacillar meningitis. Sections of the orbital contents showed a relation between the numerous small abscesses in the orbit and thrombosed orbital veins. At postmortem examination the right orbit was also found to be involved, but the process was limited to the posterior part of the orbit. *Staphylococcus aureus* was the infecting organism. A purulent rhinitis was also present so that it seemed possible that the rhinitis was the primary cause of the otitis and its complications.

GIFFORD, Omaha.

Diseases of the Skin

SKIN MANIFESTATIONS IN EXUDATIVE DIATHESIS AND ANAPHYLAXIS. A. S. SOKOLOW, Jahrb. f. Kinderh. **3**:211 (Jan.) 1926.

The skin of children with exudative diathesis in the state of an acute eruption often shows an intensive reaction to heterogeneous protein. Sokolow describes the method of testing the skin and gives a few typical case histories.

EHRMANN, Chicago.

THE TREATMENT OF PRURITUS IN SKIN DISEASES OF CHILDREN. BERNHARD BORNIKOEL, Monatschr. f. Kinderh. **36**:97, 1927.

In order to find which remedies were most effective in relieving an itching skin, the author went over all his dispensary records from 1914. Of roughly 250, he was able to use 68. The remedies studied consisted of general sedatives as well as local applications. Of the general sedatives, chloral hydrate was used as a 1 or 2 per cent solution in teaspoonful doses given every quarter of an hour or every half hour. Another remedy was bromural, in doses of from 0.3 to 0.7 Gm. The list includes barbital, carbromal, urethane, phenobarbital, and trichlorethylcarbonate. Of all the drugs tried, he got the best results with ordinary bromides. Unfortunately, there are only seven such cases, but of these five were relieved by sodium bromide in doses of 0.5 Gm. given two or three times and later reduced to 0.1 Gm. Antipyretics were not in his series.

Calcium was used in six cases in which the basis seemed to be urticaria, but without any striking effect. A number of other measures were employed, such as blood letting, injections of physiologic sodium chloride solution or sea water, injections of small doses of cow's milk and increasing amounts of atropine. In none of these was there any benefit. Interesting results were obtained with amyl nitrite. Inhalation of from two to five drops repeated for a number of days gave relief in a number of children, particularly in that group which showed the most marked vascular reaction. The treatment was limited to the exudative type of child rather than to the one with strophulus.

A salve which proved as effective as any for milder cases was one part of hamamelis water to eight parts of white petrolatum. The effect was intensified by the addition of small amounts of anesthesin or procaine.

GERSTLEY, Chicago.

A LETHAL FORM OF EPIDERMOLYSIS BULLOSA HEREDITARIA IN THE INFANT. E. JENNY, Ztschr. f. Kinderh. **43**:138 (Feb.) 1927.

Seven cases are reported of a form of epidermolysis bullosa hereditaria in which the tendency to formation of vesicles from birth was so marked that without exception death occurred in weeks or months. The mechanical origin of the vesicles, changes in the nails and ulceration of the mucous membranes

were shown by the localization, and were demonstrated by experiment. In a family tree reaching to the seventeenth century, recessive inheritance could be traced in agreement with Siemen's view of the recessive inheritance of the dystrophic form.

PAUL W. EMERSON, Boston.

Surgery and Orthopedics

CONGENITAL HYPERTROPHIC STENOSIS OF THE PYLORUS. THE RESULTS OF RAMMSTEDT'S OPERATION. SEYMOUR BARLING, Lancet **213**:492 (Sept.) 1927.

The author feels that the degree of obstruction undoubtedly varies in different cases, and that there is no method of diagnosing this accurately early in the course of a case; he feels, further, that to try medical treatment at first and then to change to operation at a later stage, when the child's condition has become worse, is to court disaster in the average case.

Of the ninety patients in this series, many were extremely wasted and ill and were poor operative risks. As a rule, before operation the infant had a few days' treatment in the hospital with rectal and stomach lavages daily and immediately before operation a saline hypodermoclysis. The anesthetic used was a mixture of ether and chloroform in the earlier forms and nitrous oxide and oxygen in the later forms.

Fifteen of the ninety patients were seen in private practice, and all of these recovered; of the remainder, thirty-six died. The author attributes the difference in the two groups to the relatively earlier diagnosis in the private cases. In a group of private cases, the average time that the symptoms had existed before operation was thirteen days; in a comparable group of patients in the hospital symptoms had existed for eighteen days before operation for the ones who were cured and twenty-five days before operation for the ones who died. Infants often lose 1 per cent of body weight each day that treatment is delayed. Of the thirty-six fatal cases, fourteen patients died within twenty-four hours of the operation, four of them bleeding from a divided muscle. In ten, no other cause but inanition and shock from the operation could account for the fatality. The average time of existing symptoms in these cases was fifty days.

Breast milk is considered the best food after operation, and the next best is lactic acid milk. Patients who run a favorable postoperative course often do not gain weight for the first fortnight.

LANGMANN, New York.

Miscellaneous

ZINC STEARATE POISONING. L. H. GOLDSMITH, J. M. A. Georgia **16**:310, 1927.

Zinc stearate dusting powder has been used extensively as a substitute for talcum powder, although it has no advantage therapeutically, and is more dangerous. The inhalation by infants has resulted in twenty-eight deaths, (21 per cent) in 131 cases reported. One infant, aged 3 months, died within one hour. The use of the powder should be discouraged, and mothers should be warned of its dangers by the medical profession.

MASHBURN, Atlanta.

STUDIES IN NATURAL ILLUMINATION IN SCHOOL ROOMS. TALIAFERRO CLARK and ARTHUR F. BEAL, Pub. Health Bull. **159**:1 (Jan.) 1926.

A study of daylight illumination was made in a typical modern public school with reference to the astronomic and meteorologic, physical and physiologic factors involved. The first are uncontrollable factors, such as season, time of day and cloudiness; the second include location and structure of the building (with special reference to window space, location and amount of visible sky vault); the third have to do with the variation of visibility on the children.

There is a minimum of both outside and inside illumination in the winter. The direction of the exposure of the room is largely responsible for the diurnal change of inside illumination. Inside illumination is also more dependent on sky brightness and visible sky vault, the latter in turn being more dependent on the extent and height of the windows than on actual outside illumination. For unilateral lighting, the windows should be on the left, extending to the ceiling and as far back of the pupils as possible; the room should not be more than 20 feet wide and the window space not less than one-fifth the floor space. Trees and other objects that reduce the visible sky vault should be at least 50 feet from the school building. It was found that the distribution of light in the room was better on the side of the building opposite the sun, i. e., distribution depends more on illumination than on actual light. Artificial lighting should be provided for at least the darker half of the room to use on dark days.

BARNETT, Chicago.

WHAT THE LEAGUE OF NATIONS CAN DO FOR CHILDREN. EDITORIAL, Rev. internat. de l'enf. **3**:323, 1927.

The interest of the League of Nations in questions of child welfare opens a new period in the history of work for children. It is true that one must not expect that the League has only to wave a magic wand and utter the word "abracadabra" on Monday for one to find on Tuesday that the situation of children has altered throughout the world. The very eagerness with which the League's activity was welcomed and the great anxiety that was shown to utilize without delay and to the full the machinery it provided, has, in fact, impeded its action. Nevertheless, the tendency to expect too much from the establishment of an international center on an official basis is, in itself, indirect evidence of its indubitable value.

The Advisory Committee for the Protection and Welfare of Children and Young People is divided into two committees, one to deal with the traffic in women and children and the other with child welfare. The questions which come up before the latter committee fall into two categories: (1) those which are international in the strict sense because the action of one country depends either wholly or partially on the action taken by another country, and (2) those which are only international in the broad sense that they are of common interest to all nations. The former category of questions may sometimes be suitably solved by the establishment of international conventions, but in regard to the latter, when common action is not possible, the comparison of methods and the interchange of information may nevertheless be of value. Of the subjects that are at present before the committee, one question from each category may be briefly discussed as illustrating its work.

In the first category is the problem of the relief and repatriation of alien children.

In certain areas the happiness and welfare of numbers of children of foreign nationality depend on a solution being found for this question. There are countries in which destitute alien children meet with great suffering and hardship because the orphanages, hospitals, crèches, child welfare clinics and other institutions are so burdened with work for their own children that they close their doors to foreign children. These children may be starving and homeless, they may be allowed to grow up illiterate, they may be refused treatment when ill and supervision when in desperate need; thus, they are driven into vagabondage and crime. A case is known to the Save the Children Fund of a delinquent and feebleminded boy who cannot be looked after in the country in which he has been living because his father, long since dead, was a native of a neighboring country with which there is no treaty regulating the methods of dealing with such cases. As the local authorities felt themselves unable even to pay the child's railway fare to the frontier, the only solution seemed to be that this should be provided from private charity; and further, it appeared

that the legislation of the country to which it was necessary to send him was such that his maintenance could be secured only by bringing him under the laws relating to vagabondage. This could be effected by allowing him, at his destination, to loiter about by himself for a few minutes in the neighborhood of the railway station, pending the appearance of a social worker who could declare that she had found him wandering about without means of subsistence.

The establishment of arrangements by which such cases of hardship would be obviated is urgently necessary, and the Child Welfare Committee has appointed a special subcommittee for the preparation of a draft "International Convention on the Relief and Repatriation of Minors of Foreign Nationality." This is a question in which the Save the Children Fund International Union is specially interested on account of the appeals for help that it receives on behalf of children who are driven from pillar to post because no one will acknowledge responsibility for their fate. It is clear, however, that their assistance should be a public charge instead of depending on the activities of a charitable society. The Union is therefore endeavoring to promote the work of the Child Welfare Committee in this direction by collecting information on the subject, and in doing so can render more useful service than by the occasional relief of an alien child.

Between many countries there already exist bilateral agreements which, however, do not always operate effectively. When they are based on the idea that each country should undertake to treat the children on its soil belonging to the other country on the same lines, one difficulty which arises is that the so-called "reciprocity" is usually illusory, as no two countries either have a similar number of children to deal with or similar provision to offer them. And the problem of extending such agreements arises from the fact that in different localities the problem presents divergent aspects. In contiguous countries such as France and Belgium, a child who is unhappy at school or at home may run away across the frontier and the question of repatriating him is much simpler than that, say, of sending back across the Atlantic a Czecho-Slovak child who has emigrated to Canada and whose conduct has proved unsatisfactory in his new surroundings.

In the second category of questions of interest to the Child Welfare Committee are those of blind children.

It would appear that in countries in which the incidence of blindness is low, blind children represent about five per ten thousand of the population (in Denmark, 4.55) but in many countries, especially, of course, in areas of hot sunshine and sand, the figure is far higher, and it is tragic indeed to think of the sum total of human misery that it represents. The children in institutions represent only a small minority. It is even the case that children are still sometimes used by adults to bring in money by begging and are sent out in rags in the rain and the cold.

Few realize, however, how much might be done both to prevent blindness and to alleviate its consequences. It is estimated that only about one sixth of blind children are blind from birth; it should be possible to save the sight of a considerable proportion of the remainder. In this direction, the United States of America is leading the way with its excellent propaganda and "Sight Saving Classes" which represent so great an improvement on the unfortunate practice of teaching blind and nearly blind children in the same classes, with the result that the remaining vision of the latter is too often destroyed. Again, the possibilities of occupation for the blind are wider than is usually supposed. Forty different branches of paid employment have been cited as suitable for the blind, but it is thought that investigation would add still further to the number.

The Child Welfare Committee is only now beginning its study of the subject, and it proposes for the present to confine itself to the question of totally blind children. It was suggested that investigations might be made under the following headings: (1) statistics and causes; (2) assistance to blind children; (3) education of blind children; (4) training of blind children and the

occupations for which they are suited. The Save the Children Fund International Union, which is in touch with the friends of the children in so many different parts of the world, would render a valuable service if it could induce its supporters to collect information on these points, especially in areas in which the problem has hitherto received little or no attention.

The cursory consideration of these two questions may serve to give some indication of some of the possibilities before the League of Nations for ameliorating the condition of children. In regard to international questions, strictly so-called, its activities appear indeed essential to any rapid advance. Another of these problems, in regard to which a draft, "International Convention." is being prepared, relates to the means of enforcing the obligations of parents and others in regard to the maintenance of children in other countries. It is more than time that steps should be taken to prevent the easy evasion of parental responsibilities by disappearing from one country into another, and the machinery of the League offers a ready means for calling attention to such evils which otherwise might long continue to be more or less tolerated. Again, the study which has been undertaken in regard to the mental and moral effects of the cinematograph may well tend to hasten and facilitate international arrangements not merely in regard to the prohibition of undesirable films but to the circulation of those which are of general value.

Passing from such questions to those matters of common interest in regard to which the League offers a natural center for investigation and research, one has only to glance at the list of subjects proposed for the next session of the Child Welfare Committee to appreciate their far-reaching importance. The "Special Agenda," it has been suggested, will include the examination of reports on juvenile courts, recreation and family allowances, and the discussion of these questions. Several further questions — the illegitimate child, age of marriage, protection of life and health in early infancy, feebleminded children, the effect of alcoholism on children — are proposed for the "General Agenda"; these questions will not be discussed, but a report will be made on the relevant information received.

In regard to all these problems, it is evident that the experience of different nations might of universal value. In every industrial country, for instance, at the present day there is a growing realization of the dangers that are incurred through the neglect of feebleminded children. Contrast their case with that of blind children. The blind children claim our pity and compassion; it is surely our bounden duty to do everything we can to bring happiness into their darkened lives. But their misery does not extend beyond a narrow circle. Feeble-minded children, on the contrary, are a social menace. It should, however, be possible to arrive at a sound policy in regard to this question; though such a policy would naturally require adaptation according to the internal conditions of different nations, in its main outlines it should be universally applicable.

In conclusion, the Save the Children Fund International Union once more calls the attention of its friends and supporters to the part which they should themselves play in rendering effective the work of the League of Nations for Children. It will be of little value for the League to undertake investigations and to accumulate information if the results obtained are to remain of mere academic interest. The scientific collection of data is the only basis for a scientific world-policy of child saving. But the foundations of a house are of little use unless the house is built. It is for social workers all over the world to build the house.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Annual Meeting, June 6, 1927

GEORGE E. BAXTER, M.D., *President, in the Chair*

GIARDIA INTESTINALIS INFECTION. DR. M. G. PETERMAN.

The cases of two children who had infections due to *Giardia intestinalis* are reported. This parasite was first described by Lambl and is found in the stools of children. Lambl considered the organism pathogenic in some cases of intestinal disease in children. Since that time some consideration has been given to this organism in the literature, principally by parasitologists rather than by physicians. Few physicians consider *Lamblia intestinalis* as an infectious agent. Abt's system of pediatrics does not include anything on the subject. At the meeting of the Central States Pediatric Society, Zahorsky reported five cases.

The parasite is usually found in the stools in the shape of a pear or a beetle, from 5 to 10 microns wide with from two to four nuclei on one end, and the flagella can sometimes be seen in the ova. Sometimes chromosomes are seen in the ova stage. There is a sucking disk at one end and four pairs of flagellae. The parasite is usually found in the duodenum; it becomes encysted on its passage through the intestinal tract and is found in the encysted form.

CASE 1.—A boy, who was brought to the hospital because of multiple burns of the body, was making an uneventful recovery when he suddenly became irritable and obstinate and developed anorexia. The nurse made a note thirty-two days after his admission to the hospital that the stool was offensive. Instead of one or two normal stools, the following day he passed two stools that were soft and green. Examination showed numerous cysts of *Lamblia*. The following day he refused all food, vomited twice and passed four stools that were green and yellow. In these stools were found numerous flagellate forms of *Lamblia* but no cysts.

The child continued to pass three or four green or yellow stools a day, all containing numerous *Lamblia*. He was placed on a starvation diet with gruel and liquids, without any effect. Then he was given 1 grain (0.065 Gm.) of stovarsol before breakfast each day for four days. On the second day he passed only two stools, which were brown and contained cysts. The previous stools had contained pus cells and mucus but not blood. On the third day pus and mucus were not present, but a few cysts of *Lamblia* were found in the one normal brown stool that he passed. His appetite had improved. He was no longer cross or irritable, but contented. He did not show further symptoms while he was in the hospital; he gained weight and ate well, but when he left the hospital the stools still showed a few cysts of *Lamblia*. He returned for observation and did not have further diarrhea or trouble of any kind.

CASE 2.—Muscle spasm or diarrhea were not present in a boy who complained of some obscure abdominal distress; there was nothing to explain indefinite abdominal pain, nausea, anorexia and the tendency to vomit once every two or three days. Examination of the stools showed numerous cysts of *Lamblia*. The boy remained in the hospital for three days and was then taken home, under protest, to return three or four days later with a return of the trouble.

On his second admission, he developed mumps and was put in isolation. He then developed otitis media and was not treated for the *Lamblia* infection. He did not report again for observation.

Eosinophilia was not present in either case.

During the past year, the stools of 112 children have been examined whenever anything suggested an intestinal parasite, but a parasite was found in only seven. Four of the stools showed infections with *Lamblia;* two of the children did not have enteric symptoms and the other two have been described.

In the *American Journal of Hygiene* (Hill, C. M., and Hill, R. B.: Am. J. Hyg. **7**:134 [March] 1927) the Hills stated that in the 57 per cent of the children of Porto Rico in whom intestinal parasites were found, *Lamblia* was found in 47 per cent. These children gave a history of recurrent diarrhea through the year.

Lamblia intestinalis must be considered as a definite causative organism in many cases of intestinal disease.

PELLAGRA. DR. E. T. MCENERY.

A Mexican boy, aged 1 year and 9 months, had lesions of the skin in the form of exfoliating dermatitis which started on the thighs and knees and spread to the hands, face and lower extremities. The child's father has been at the Oak Forest Sanitarium, where he had been treated for tuberculosis, although organisms were not found. At the time the child was examined the father was working for a railroad and apparently was in good health.

The child's birth was normal, and lesions of the skin were not present. During his stay in the hospital, the Social Service history was ascertained. The child was fed on breast milk for nine months, then on certified milk with cane sugar four times a day. He was also given white and bran bread, applesauce and, occasionally, soups, but there was no history of his having received meat or vegetables.

On admission, the child showed marked exfoliating dermatitis with scaling. All the hair had started to fall out when he was about 1 year old, and the father had shaved it off. Since then it had never regrown. The child had bilateral ectropion and photophobia. The skin bled easily. All the lesions had a scaling margin, with a typical lesion of pellagra on the neck in the form of Casal's collar which extended down on the back of the neck. The lesions on the abdomen extended almost to the xiphoid process. The lesions were absolutely symmetrical, and a gauntlet-like lesion was present on the hands and wrists.

The blood picture was practically normal. Roentgenograms of the chest revealed a normal condition. The examination of the stool was negative, as were the blood Wassermann and Pirquet reactions on two occasions.

DISCUSSION

DR. JOSEPH BRENNEMANN: There is one interesting feature in this case which I think should be stressed. I had seen only one case of pellagra before and that was in a colored child, who was admitted to the Children's Hospital in the first stage of pellagra, with erythema. The disease had reached the desquamating stage. The dermatologists had seen the child first and had thought that the condition was a disease of the skin. Dr. McEnery served his internship at the Cook County Hospital and recognized the pellagra because he had seen another case of it. Pellagra is not common in young children, although Ross Snyder says that he has seen several with it and that they nearly always recover. One of the things he emphasizes in his article in Abt's "System of Pediatrics" is the frank symmetry. He says that if the lesions are not symmetrical, the disease is not pellagra. This symmetry was striking in the case reported and helped establish the diagnosis. Two or three weeks ago, the condition was more convincing than at present, for then it

was in the reddish-purplish stage that unquestionably is pellagra. The child was shown before the Dermatological Society and the question of acrodynia was brought up, but the only symptoms of acrodynia were the profuse nasal discharge and unhappiness. The case is unquestionably one of pellagra and is interesting because of the age of the patient.

A Case for Diagnosis. Dr. F. J. Corper.

Robert S., aged 7, was taken sick one morning with a high temperature and extreme drowsiness. He vomited once or twice during the day, refused all food and water and fell back into a stupor after being aroused. His only complaint was that of being tired.

He was seen that evening, about ten hours after the onset, and was found to be fairly well nourished but in an extremely toxic state. The results of the examination were negative, except for a temperature of 105 F.; he could be roused from the stupor caused by the fever only to talk rationally. A marked hyperemia and apparent swelling of the membranes of the pharnyx and soft palate were present. The tonsils had been removed a month previously. Adenopathy was not present. The reflexes were normal.

The second day the child seemed much brighter, although the temperature still hovered around 104 degrees and the throat was bright red and swollen. The skin was normal.

On the third day erythematous, swollen and velvety blotches appeared on the trunk and limbs, mostly on the volar surfaces. They were as large as the palm of a hand and irregular in outline. Normal areas of skin were present between the patches. The temperature was still high, the throat was highly inflamed, and the child was in a highly irritable and excited condition.

In the course of the next twenty-four hours, the patches assumed cresentic and circinate forms; some of them coalesced and formed patches as large as a small plate, and the child complained of extreme pain and sensitivity of the entire surface of the body.

By the fifth day, vesicles or bullae had appeared on practically all of the patches, which now covered almost the entire surface of the body. The mouth became so swollen that the child refused to swallow or even to open his mouth. He vomited repeatedly and developed a diarrhea, passing blood-streaked mucus.

In the next few hours most of the bullae ruptured, freeing a light yellow, slightly turbid fluid and leaving raw, inflamed surfaces. The child sank into a comatose condition, and scarcely responded to stimulation. More denuded areas appeared on the body, and for the remaining days of his life he lay in an unconscious condition, his tissues dehydrated and his body giving the appearance of having been scalded with hot water or steam.

He died on the tenth day. Autopsy was not obtained.

The diagnosis of the condition is simple if one regards the manifestations of a disease of the skin as a complication of the infection of the throat. The diagnosis of the condition, according to the lesions of the skin and membrane, seems more difficult, and seemingly is the subject of controversy.

The case appeared to be one of a severe overwhelming infection of the throat with enough toxemia or bacteremia to involve all of the organs and tissues of the body. The vomiting, the diarrhea and the presence of blood and casts in the urine are enough evidence that tissues other than those of the skin were involved. The white cell count of 9,000, taken on the third day, is evidence of the severity of the infection and the degree of resistance of the child.

Ordinary scarlet fever, which was at first suspected may be ruled out by the later manifestations.

So far as the manifestations of a disease of the skin are concerned, by far the most likely diagnosis would be erythema multiforme with bullous formation or erythema bullosum. This is presumed to be a toxic condition accom-

panied by ring-shaped or circinate lesions which later were surmounted by vesicles or loose bullae containing blood or serum. The distribution was symmetrical; it was apparently more common on the dorsal surfaces, and the course was more or less chronic rather than acute. However, I have seen two patients with so-called erythema multiforme with bullae. The onset was acute in both instances, with high temperature and prostration and a course of two or three weeks with progressive improvement. Neither case showed the denudation of skin and the severe constitutional symptoms of the one described.

In pemphigus, one encounters a severe infection of the skin manifested by the formation of bullae containing bloody serum and apparently appearing on a normal base rather than an erythematous or swollen one. Denudation of the surfaces with failure to heal is more common than in erythema multiforma. Constitutional symptoms, however, are severe and the prognosis is bad. In this disease, there is usually a definite focus of infection and the mucus membranes may be involved. In the case described one might presume that the throat was the focus of infection.

Other diagnostic possibilities include dermatitis exfoliativa and even the foot-and-mouth disease. In dermatitis exfoliativa, however, one finds a widespread exfoliation of most of the body without the bullous formation, and the constitutional symptoms are generally slight. In this disease the superficial layers of the skin are slowly detached and left on the surfaces in the form of small, flake-like particles.

In the foot-and-mouth disease there are congestion and swelling of the membranes of the mouth with the formation of vesicles and severe constitutional symptoms subsiding with the exanthem. The entire body may be affected, although the eruption is generally limited to the mouth and the soles of the feet. The disease is self-limited and not fatal.

The condition in the case reported was diagnosed as erythema multiforme bullosum by one dermatologist and by another as pemphigus. I am inclined to accept the former diagnosis, being prejudiced by the fact, possibly, that the diagnosis of pemphigus was made on first glance on the sixth day of the illness and without allowing me to describe the onset of the disease to the consultant.

INTERTRIGO; HERNIA. DR. ROBERT BLESSING.

In an infant born on March 19, 1927, the weight at birth was about 6 pounds (2.7 Kg.). Marked cyanosis was present for several hours after birth, and oxygen was administered. He was sent home on the tenth day and was fed breast milk with a supplementary feeding of protein milk. On March 31, a right inguinal hernia suddenly appeared and descended into the scrotum. It was easily reduced. At the age of 5 weeks, the child weighed 7 pounds 12 ounces (3.5 Kg.). A marked intertrigo of the perineum and inner surfaces of the thighs, with apparent itching, was present. A soothing lotion with 1 per cent phenol was prescribed, and the mother was instructed to leave the parts exposed to the air as much as possible. The stools at this time were semisolid and satisfactory. The hernia came down every day or so and seemed extremely painful but was easily reduced each time by the mother. No attempt was made to apply a truss.

On April 25, two days after the first application of the lotion, the infant passed brownish-black urine, in small amounts, with pain. A brownish-red discoloration of the diapers had been noticed after two or three applications, and the use of the lotion had been discontinued within twenty-four hours; six applications had been made. The child vomited after each feeding and passed seven or eight loose, watery stools in twenty-four hours. He refused to nurse, was afebrile, showed an intermittent dusky cyanosis, was fussy and objected to handling. The hernia was not down, and the lesions on the skin were markedly improved. Eight cubic centimeters of brown-black urine was collected. The mother said that it was dark when voided and became darker

on standing. It was black when viewed in an indirect light. It was acid, did not contain albumin and did not reduce Fehling's solution. Tests for bile, acetone, indican and blood were negative. Microscopic examination showed nothing abnormal. The bismuth chloride precipitation test for phenol was strongly positive. The following day the urine was said to be clear; a specimen was not saved. The infant cried a great deal, nursed poorly and passed frequent loose stools. The next day there was no breast milk, and protein milk was well taken. A specimen of urine taken on the same day was normal in every respect. The stools soon became normal. The intertrigo persisted in a mild form, and the inguinal hernia required the use of a yard truss, which seemed to be successful.

HEART BLOCK. DR. STANLEY GIBSON.

In March, 1923, a child was brought to the Northwestern University Medical School Dispensary because of some intestinal trouble and loss of weight and appetite. At that time physical examination disclosed that the heart was slow and regular, the rate being 50. In addition to the slowness a murmur was present, maximum over the third and fourth left interspaces, and the heart was slightly enlarged to the left. A roentgenogram made at a distance of 7 feet showed the cardiothoracic ratio to be 52 per cent. The child was apparently in good health, but on close questioning it was found that she was not as active as other children; she did not take part in strenuous games but on taking her own time she got along well, and her mother had never appreciated that she had any heart trouble. There was a flush on her cheeks that at first glance made her look healthy but that on study suggested cyanosis. The family moved away from the city for a time but moved back, and the child returned to the dispensary about three months ago. The heart rate was still 50; so the condition must have been present for four years at least.

An electrocardiogram at the time of the first visit showed complete heart block and in addition a sino-auricular block. Dr. Carr of the Wesley Memorial Hospital saw the electrocardiogram and said that he had never seen another like it. The electrocardiographic study was repeated at Wesley Memorial and at St. Luke's hospitals, and both studies showed heart block but no sino-auricular block.

One cannot conscientiously say that this condition was congenital heart block, but at least it was a permanent, complete heart block, probably congenital. Few conditions will produce a complete heart block; diphtheria will do this, but there is no history of the child having had this disease. The symptoms were those one would expect in a defect of the interventricular septum, and with the cardiographic evidence of heart block one is safe in saying that such a defect was present and had interrupted the auriculoventricular bundle. Paul White reported one case several years ago and another recently, and in addition cited seven or eight from the literature. I have heard of another case and hope Dr. Aldrich will say something about it.

The only other interesting fact was that the child was sent to Sunset Camp for rest and recreation. A short time afterward the physician there telephoned me and told me that the girl, who was then 13, had developed acute rheumatism. I asked him to send the child back, and she was admitted to St. Luke's Hospital. She had a temperature of 103 F., and her throat was sore. She is now comfortable, and I have not been able to note any change in the condition of the heart due to the possible development of an endocarditis.

DISCUSSION

DR. C. A. ALDRICH: I have had a similar case in a child whom I first saw at 4 years of age, during the epidemic of influenza in 1918. Her temperature reached 105 or 106 F. and the pulse rate was 45. The history, as obtained from the mother, was that the child had had a congenital heart defect. I

telephoned Dr. Abt, who had seen the child at birth, and he said that she had a congenital heart defect of some sort but that he was not sure what the lesion was. She made a good recovery from the acute infection. I saw her subsequently many times with and without infections, and she always had the slow pulse. She played all sorts of games and did not have dyspnea, although she may have had slight flushing or cyanosis. She played basketball, went swimming and did everything other children did. When she was 12, her mother asked if they should allow her to do all the things she was doing. I thought that it was time to make a definite diagnosis, and so had an electrocardiogram made and found a 1 to 3 heart block. I did not like to restrict all of her activities, for she had never showed any dyspnea or tiring. My consultant on the case agreed that the difficulty was due to poor conduction rather than to poor muscle and that it was not necessary to take the child out of her accustomed activities, although she might have difficulty from the defect in conduction. He recommended that she be allowed to play but that she be kept out of the most violent kinds of competitive sport. I had some difficulty in carrying this out. She went to camp the next summer and, while standing in the water before swimming one day, dropped dead. Postmortem examination was not performed; but I think that unquestionably this was a case of congenital heart block and that the impulse did not go through at the time of death.

DR. JOSEPH BRENNEMANN: I have an idea that if one keeps looking for peculiarities of this sort in children one will find more now than were found before the present instruments of precision were available. I saw a patient in Washington, D. C., whose condition was much like the one just described by Dr. Aldrich and who had a constant pulse of 51. The intern said that there were thirty-two cases on record but that only seven had been definitely established as heart block. The child that I saw was cyanotic and acted in every way like she had congenital heart block; I had the same idea that Dr. Gibson had regarding his patient, namely, that there was a defect in the interventricular septum. I have a patient now, an infant, whose pulse suddenly leaps up to 220 or so and after a while goes back to normal, where it stays most of the time. Dr. Baxter and I saw a new-born infant at the Presbyterian Hospital who had a similar condition. As I listened to the heart, I heard a purring sound over the base; as I listened further out to the apex, the rate was about 160. Dr. Baxter saw the child later when the heart beat was still rapid, and he gave a little digitalis. Within a day or two the heart became normal, and the child never had any further trouble. I think the child had an auricular flutter, which might be distinguishable in a new-born infant with a thin chest wall.

EXPERIENCES WITH SCARLET FEVER SERUM. DR. MARK JAMPOLIS.

I wish to relate a few of my experiences with scarlet fever serum. I do not intend to convey the impression that I am condemning the use of the serum, for I have not used it in a sufficient number of cases. Nevertheless, my percentage of disappointing results has been so high, so different from what I had anticipated, that I am now afraid to inject it under almost any circumstances. I wonder if others have had similar experience.

A boy, aged 3, developed a suspicious rash. His uncle, a physician, administered the Dochez serum. Within a minute or two, the child collapsed and appeared dead. Intracardiac injection of epinephrine restored heart action, and when I saw the child a half hour later he was barely living. The rash rapidly disappeared and severe cutaneous reactions developed with dyspnea and hyperpyrexia. After about five days had passed, the child was on the way to recovery. This child had received diphtheria toxin-antitoxin at 1 year of age.

I sent another child with pneumonia to the Sarah Morris Hospital. The resident physician called me late that night and said that a scarlet fever rash had appeared. My assistant agreed with his diagnosis, administered the Dick serum and sent the child home. Next morning there was no sign of a rash,

the mucous membrane of the mouth and pharynx was pale, the parents did not believe that the child had scarlet fever and I was discharged from the case. The child died that night, and the physician who treated her informed me that the symptoms of serum reaction were more pronounced than the pneumonia.

I saw a physician's child who had a slightly inflamed throat accompanied by vomiting. The condition seemed to be mild grip. On the third day the typical rash of scarlet fever appeared. The father, who had been visited by a detail man a few days before, suggested that we use a concentrated Dochez serum and I agreed. At 2 p. m., before the serum was given, the temperature was 103 F., and the constitutional symptoms were not severe. At 2 a. m. the next morning the temperature was 106 F.; a severe angina, enormous enlargement of the cervical lymph nodes, and a less marked general adenitis were present. The rash had disappeared, and the child was in a deep stupor. Death occurred the next night at the Contagious Hospital. This child had not received toxin-antitoxin for diphtheria.

I then saw a child who had received an injection of prophylactic serum in Kansas City. I saw him two days later, when he had a temperature of 105 F., severe dermal disturbances, painful swollen joints and extreme prostration. Hyperpyrexia continued for five days.

I also saw another child, whose condition ran a similar course and who had received an injection of prophylactic antitoxin at the Dick laboratory. He had high fever for five days and more dermal disturbance than I have usually seen in reactions from diphtheria serum.

I gave the Dick serum to three children in one family on the first day that the Squibb serum was on the market. One child was given the serum on the second, one on the third, and the other on the fifth day of the disease. The one given the serum on the fifth day developed otitis media, the one on the second day, a streptococcic infection of the hand, and the one given the injection on the third day ran a course apparently unaffected by the serum.

A week ago, two mothers in the same apartment building called to consult me about giving serum to their children who had been exposed to scarlet fever. I hesitated, then advised them to take a chance and not give the serum. Then I began to worry. On the same day, Dr. Schutzbank called me to see a patient who had developed a typical scarlet fever rash for the second time seven days after the serum had been injected, accompanied by high fever and symptoms of severe sepsis. Dr. Schutzbank will discuss this case. I was glad afterward that I had not given the prophylactic injections, as the children did not develop scarlet fever.

I can recall one brilliant result. In a child with a pronounced rash and a temperature of 102 F. the rash disappeared within a few hours after the injection. The fever disappeared the next day, and the mother has never believed that her child had scarlet fever.

I do not know whether my experience is unique; I do not want to appear unprogressive, but my experience in these few cases has naturally made me dubious about giving serum. During the same period, I treated probably as many patients without serum. They had fever for a week or two; some developed adenitis, but none had severe complications, and all recovered.

DISCUSSION

DR. F. B. SCHUTZBANK: The girl Dr. Jampolis mentioned was 12 years old and was seen about noon on May 9, when she gave a history of sore throat and vomiting. The throat was red and injected, and the tip of the tongue had a strawberry appearance. The temperature was 100 F., the pulse rate, 84. The body presented a typical scarlet fever rash. She was not very sick but was given a therapeutic dose of Squibb's antitoxin. That night the temperature went to 103 F. but diminished the following morning, and the child's condition was satisfactory for a few days. When I saw her the fifth day, she complained

of feeling ill. The joints were tender and urticarial manifestations were present all over the body. The temperature went up to 104 F.; all of the lymph glands were enlarged and were tender and painful; the rash was very marked; the child was nauseated and vomited everything taken by mouth. The following day the symptoms were the same, and the temperature was still 104 F. The same symptoms persisted on the third day. Following hypodermic injections of atropine and epinephrine hydrochloride, some of the rash disappeared. The next morning at 5 o'clock the child appeared much worse and was restless. The temperature was 105 F., the pulse around 160 and the lips and fingers were cyanotic. The body was covered with the marked rash of erythema multiforme, and between the patches of erythema one could see practically every kind of urticarial manifestation. The glands, however, had decreased markedly in size and were not so tender and painful. The child was given epinephrine hydrochloride and morphine and slept; she awoke at 2:00 p. m., feeling better. The next day the temperature was 101 F., and she then made an uneventful recovery. The blood count revealed 21,000 leukocytes. The past history was negative, except that she had received three injections of diphtheria toxin-antitoxin in November, 1923. She had not had hay-fever, hives or asthma.

DR. CHARLES SCHOTT: About two years ago, I gave a child with scarlet fever a therapeutic dose of serum. I gave the child's brother and mother prophylactic doses. The condition of the patient with scarlet fever progressed satisfactorily, but about five days later, the other child and the mother broke out with a marked reaction. One night, the mother could not speak and had no way of calling me. I gave her epinephrine hydrochloride in the morning and she became better. The condition of her throat was typical of that of scarlet fever, but the rash was not present; the infant developed a rash and all the other symptoms. This spring a cousin of the patient developed scarlet fever, and I gave a prophylactic dose to my patient. He broke out the next day with severe urticaria and adenopathy in which the glands in the neck, axilla and groin were as big as oranges. This condition persisted for five days, with a temperature of 105 F. I did not give the serum to this boy's older brother for he had had scarlet fever several years previously; however, he had another attack about three weeks later. The younger child was sent away for four weeks. He came back the day quarantine was lifted and developed scarlet fever, dying of meningitis six weeks later. At the height of the anaphylactic process I telephoned Dr. Dick and asked him what I should do; he said that the prophylactic doses should not be given any more.

DR. CLIFFORD G. GRULEE: History repeats itself. Jenner had just such criticisms of his vaccine. Everything that has been mentioned as fatal can be put on the basis of anaphylactic reaction. In judging the scarlet fever serum one must take into consideration the fact that nearly all the children have been given toxin-antitoxin. I saw a form of reaction probably as severe as any of these in which a wooden-like migrating edema, which came from diphtheria antitoxin given after the child had had toxin-antitoxin, was present, I have not had enough experience with scarlet fever serum to have an opinion to offer, but it seems to me that it must be decided whether the scarlet fever antitoxin is giving results in scarlet fever, and then these patients must be protected against anaphylactic reactions. Scarlet fever serum is still in the experimental stage. It will take several years for it to be developed so that it can be depended on and, in the meantime physicians should be careful how they condemn it because of purely anaphylactic reactions, usually on the basis of the fact that toxin-antitoxin has been given.

DR. PERRY WOOLERY, Heltonville, Ind.: I wish to give the experience of a country practitioner, with a child who had a temperature of 105.5 F. and convulsions. At 7 p. m., I gave a therapeutic dose of serum. In the morning

the rash had almost disappeared, and two or three days later the child was well. A little later I gave another child a therapeutic dose of serum, and within a short time that child was well.

Dr. S. C. Henn: I recently had occasion to give thirty-eight prophylactic doses of this serum. All the children had received toxin-antitoxin from one to six months before, probably thirty at least three months before. Only about six in this group had any reaction. Three developed a slight rise in temperature within a few hours, and three developed a slight rise in three or four days. I had been seeing three or four children with scarlet fever every day, and for that reason gave this group of children the serum.

Dr. Franklin J. Corper: About a year ago, I reported a series of cases much like those of Dr. Jampolis. Since that time, I have used the serum more sparingly and therefore have not seen any ill effects except in one case. About two months ago, I saw a boy, aged 6, who had a severe form of scarlet fever. He had been sick one day. I injected about 1 minim (0.06 cc.) of the serum intracutaneously and left the house, expecting to return in an hour or two. I was almost immediately recalled and found the child in the throes of an anaphylactic shock. He was almost in coma; the respiration was rapid and shallow, with wheezing and foaming at the mouth. The body was covered with large reddish, purplish wheals. The chest was filled with râles, and the heart sounds were so rapid I could not count them.

The boy was given 15 minims (0.92 cc.) of epinephrine hydrochloride and 1/150 grain (0.4 mg.) of atropine. In a few minutes the respiration improved, and some of the wheals disappeared. Three days later, most of the anaphylactic symptoms had disappeared.

I quote this case to show what harm may be done a sensitive patient by as little as 1 minim of serum and to emphasize the importance of tests in patients who may be sensitive. The mother said that this patient had not had a previous injection of serum.

Dr. M. G. Peterman: I have used this serum in a small number of cases and have given seven or eight injections to nurses. A few weeks ago, soon after an injection, a nurse developed a severe angioneurotic edema, with involvement of the mouth and mucous membrane, edema of the glottis, spasm with rigor of the facial muscles and great pain from contraction of the facial muscles and the hands and feet. I think that the reaction was purely anaphylactic, but I do not believe that the eruptions on the skin and the sore throat that have been described as following injections of serum could be symptoms of anaphylaxis.

Dr. Louis J. Halpern: I have used this serum in about fifty cases of scarlet fever, and the symptoms resulting from its use varied from a slight rise in temperature to polyarthritic manifestations sometimes associated with purpuric eruption. All of these patients recovered from the serum reactions. In all patients with severe forms of scarlet fever seen early in the course of the disease, or later, when they had developed complications, especially in the toxic and septic types, the use of serum therapeutically brought the fever down and hastened recovery.

Massive Collapse of the Lung in a New-Born Infant. Dr. A. H. Parmelee.

Infant B., born Feb. 22, 1926, was first seen when it was 2 days old, on account of severe dyspnea. Labored breathing had been noticed for the past twenty-four hours but had apparently not been noticed during the first day.

On inspection, the infant looked pale and exhausted but not definitely cyanotic. The respirations were rapid, and the pulse rate was rapid but strong. Percussion showed impaired resonance over the entire right side of the chest, while the left side of the chest was tympanitic. Auscultation revealed

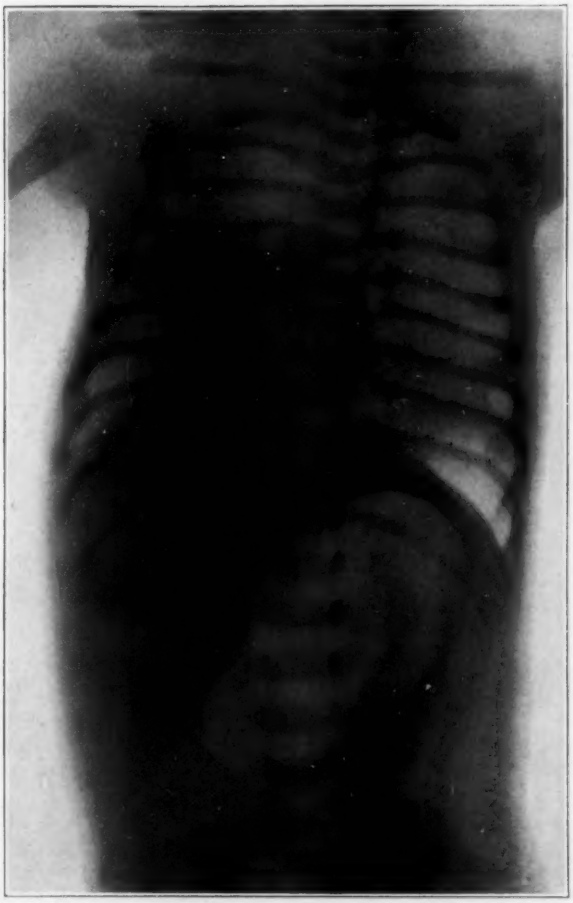

Fig. 1.—Roentgenologic appearance on second day after birth.

that the heart sounds were best heard to the right of the sternum; the apex impulse could not be felt because the apex was substernal. The heart sounds were normal.

It was evident that the heart was displaced to the right, and my first impression was that I was dealing with a diaphragmatic hernia. However, a roentgenologic examination on the same day revealed the following interesting picture (fig. 1): the heart was pulled strongly to the right, together with the great vessels; a line, which seemed to be that of the pleura, was plainly seen

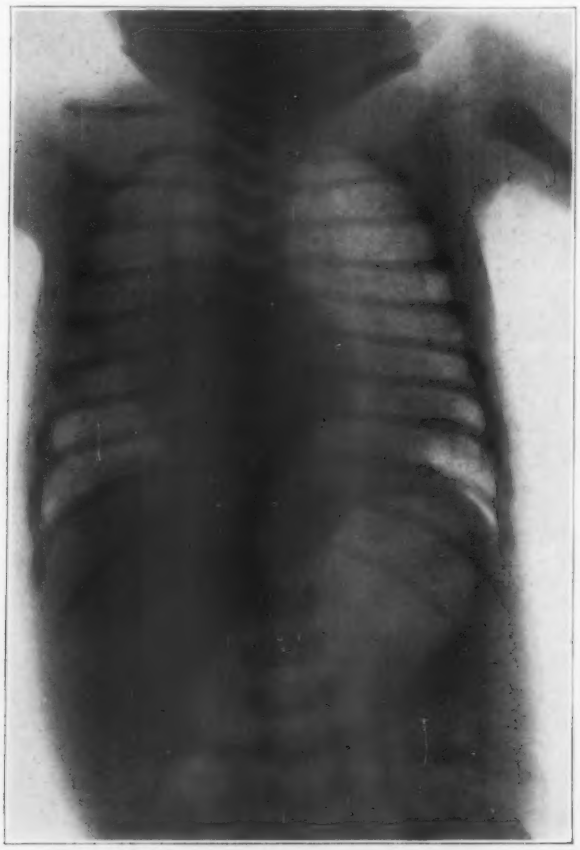

Fig. 2.—Roentgenographic appearance on third day after birth.

on the left extending from the apex to the diaphragm and being at least 1½ inches (3.7 cm.) from the chest wall as if the parietal and visceral pleura had been completely separated. The diaphragm on the left was flattened and depressed in comparison to the right.

The following day the infant was distinctly more comfortable and breathed wih less difficulty. The roentgenogram made on that day (fig. 2) showed that the heart was not displaced so far to the right and that the line of pleura on the left was not so far from the chest wall.

A third roentgenogram taken about ten days later (fig. 3) showed that the heart was in practically a normal position; the line of pleura on the left could

no longer be seen, but on the right the pleural margin of the lung was separated a distance of from ½ to 1 inch (1.2 to 2.5 cm.) from the wall of the chest, as if the right lung which had been collapsed had not yet become completely inflated. The infant improved steadily, and when last seen at the age of 2 weeks, seemed normal.

I report this case because I have found few cases of massive collapse of the lung in new-born infants reported in the literature. I consider that the condition probably is due to a complete blocking of the right bronchus by aspirated mucus or food.

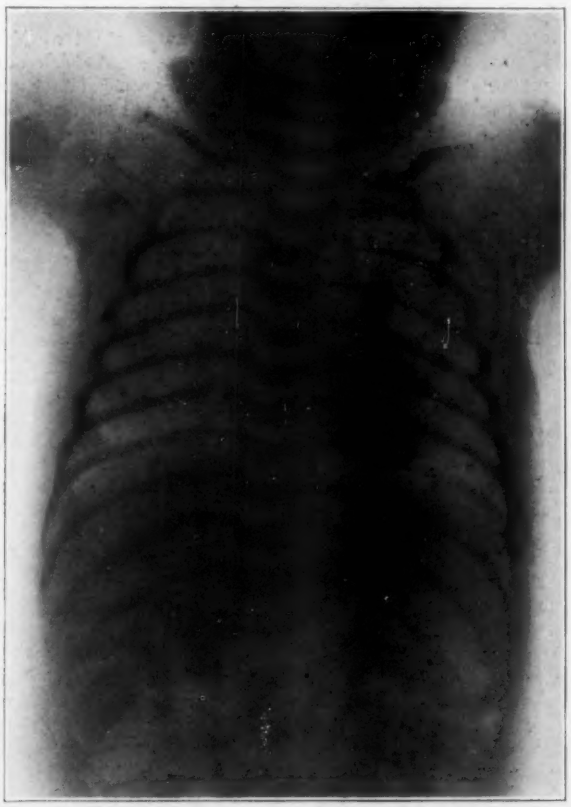

Fig. 3.—Roentgenographic appearance thirteen days after birth.

UNILATERAL EXOPHTHALMOS DUE TO ORBITAL HEMORRHAGE IN A NEW-BORN INFANT. DR. A. H. PARMELEE.

Infant W., born Feb. 15, 1927, was examined on the first day of its life, and nothing unusual was noted. On the second day, the nurse noticed that the right eye was protruding. The following day, the intern recorded on the chart that the right eye was bulging and called in the attending ophthalmologist, who examined the fundus and found it normal.

On the seventh day I examined the infant again, and the eye was definitely less prominent than on the fourth day when last seen. I made the following notation on the record: "In view of the fact that no exophthalmos was noted until the second day, that it increased steadily until the fourth day and is

now definitely spontaneously subsiding, and also on account of the ecchymosis noted on the lids on the fourth day, it seems most probable that hemorrhage into the orbit similar to that which occurs, at times, in scurvy was the cause of this unilateral exophthalmos."

The infant was brought back for observation on May 14, 1927, when it was 3 months old, and there was no evidence of any trouble with the eye. Photographs taken on the fourth day showed the exophthalmos plainly, while a photograph taken at 3 months showed that the eyes were normal.

This was a case of orbital hemorrhage due to trauma in delivery which caused unilateral exophthalmos.

DISCUSSION

DR. GRULEE: I think that Dr. Hess and I saw a child at Michael Reese Hospital whose condition was similar to that in Dr. Parmelee's first case. On roentgen-ray examination, a lung shadow was not seen. The whole area was as dense as the heart shadow. The child lived for two or three days, and at autopsy we found that the lung was completely atelectasized.

DR. JOSEPH BRENNEMANN: The first child was 2 days old when the maximum symptoms appeared. I wonder how a congenital atelectasis could be ruled out.

DR. PARMELEE: The heart would not have been pulled over so strongly if negative pressure had never been present there.

DR. BRENNEMANN: I have not seen any case of collapse in which the shadow of the heart was not much more dense than in these pictures. I doubt whether there is such a thing as a drawing of the pleura away from the wall of the chest.

CHOREA. DR. JESSE R. GERSTLEY.

This typical case forms one of a group which I reported recently before the Illinois State Medical Society. The object of that report was the demonstration of the importance of social service work, and of mental factors in the conduct of a case. In addition, the study showed that removal of the tonsils did not have any effect on the course, duration or recurrences of the disease. However, tonsillectomy seemed to diminish the number of cardiac complications. The study suggested that the relation of chorea to infection might not be as close as was formerly thought. The case that I shall describe may demonstrate the other side of the argument and furnish a clue to the infectious etiology of the disease.

Four years ago, a boy, aged 11, had an attack of chorea and was discharged from the hospital as cured. The following year he developed another attack and was again discharged as cured. A year later, he developed a third attack, and this time was discharged to the convalescent home. After four months, during which improvement did not occur, I heard of him and asked that he be readmitted to the hospital. Examination showed that his case was an ordinary one. Routine examination by Dr. Tigay showed a negative blood culture as well as normal blood chemistry. Routine determination of electrical reactions revealed a slight increase in irritability. Specialists found that the nose and throat were normal. The tonsils had been removed years before, and the sinuses were normal.

The social service investigation gave interesting information. The boy's mother was morose. The more nervous he was, the more she "picked" on him. On the other hand, the attachment between him and his father was especially strong, and the death of his father seemed to have precipitated the last attack. With this as a clue, I spoke to him of his father's death. His emotional reaction was profound, and, although he had been lying quiet, he showed at once the physical signs of an acute chorea. This experiment was repeated a number of times. Whenever his father's name was mentioned, he burst into tears and choreiform movements became marked until he had quieted

down again. In an attempt to occupy his mind with other thoughts, he was placed in a wheel chair and was given school work. He improved markedly for a time, but then seemed to suffer a remission. With the mental factors still in mind, I questioned him again and found that the anniversary of his father's death was to occur within a few days and that he wished to go home to say prayers. When assured that he might, he became better rapidly.

There is another side to this picture. The boy's emotional reactions seemed more profound than in most cases of chorea. I learned that he had severe headaches at the time of the second attack. During the second attack and ever since, he had seen double. He had been examined by an ophthalmologist and a neurologist, who confirmed the possibility that this may have been a case of encephalitis. With the exception of diplopia, there were no other symptoms to confirm this diagnosis. The spinal fluid was normal.

This may be a borderline, a sort of "missing link," case. Many are convinced that chorea is an infectious disease. Encephalitis, which is also considered an infection, frequently is associated with choreiform manifestations. This boy seems to be a link between the two conditions. Can one draw the suggestion from this case that the two diseases are related?

ACUTE TOXEMIA; MENINGITIS; DIARRHEA. DR. RALPH H. KUHNS and DR. PERKINS.

A child, aged 1½ years, was admitted to the children's Memorial Hospital on March 26, 1927, with a complaint of nausea, fever and convulsions. The birth had been normal, and the child had seemed well until the night before admission to the hospital. She had played in the park and had apparently been in good health on March 25, but she became restless after midnight. The mother gave an enema, which quieted her somewhat. At 4:00 a. m., she began to stiffen and was in almost continuous convulsions until admission to the hospital. The temperature was 104 F. at 5:00 p. m. She was not stuporous, but apathetic. The neck was not stiff and the Kernig and Brudzinski signs were not present. The eyes were turned to the right but could be moved in all directions. The pupils were large and reacted sluggishly to light. The throat was reddened. The left ear drum was pink but not bulging; the right ear was filled with wax. The chest was resonant, and the breath sounds were diminished over the right base posteriorly. Râles were not present. The knee reflexes were sluggish but present. The spinal fluid was clear and was under slight pressure; 10 cc. was removed. The cell count was 3, and culture showed staphylococcus. The blood count revealed 5,000 white cells. The urine showed some pus. A catheterized specimen two days later was yellow, cloudy and acid, with some albumin but no sugar. Microscopically, it was loaded with bacteria. The organism present was probably *B. coli.* The child passed large diarrheal stools, with large curds and much mucus. A tentative diagnosis of infectious diarrhea was made, and two days later she was passing green, bloody stools with much mucus. The temperature was 104.4 F. but soon fell to 101.8 F. When seen at 8:00 a. m., on March 29, the child's face was drawn, with a tendency toward cyanosis. The eyes were wide open, the pupils were dilated and the eyes and head turned to the left. When the patient was lifted preparatory to applying a mustard pack, she became rigid. There was slight reaction to the pack. Other measures were unavailing, and the child died at 11:40 a. m. Necropsy revealed a septicemia caused by *Streptococcus viridans;* an extensive subdural hemorrhage on the right, with scattered foci of intra-pia-arachnoid hemorrhage; multiple hyperemic points in the colon; secondary anemia, and postmortem perforation of the stomach.

Book Reviews

PATHOGENESE UND THERAPIE ALIMENTARE KLEINKINDERANÄMIEN MIT BESONDERER BERÜCKSICHTIGUNG DER SOGENANNTEN "ZIEGENMILCHANÄMIE." By H. BAAR. Price, 2.20 marks. Pp. 44. Berlin: S. Karger, 1927.

Baar, who is an assistant in Monti's clinic in Vienna, presents in this brief monograph, a complete discussion of the literature of the nutritional anemias of young children, with some clinical observations and experimental studies of his own. The first few pages are given to a discussion of anemia from iron starvation, with an attempt to clear up some confusion of terms in the literature. Baar would have the condition known as "Pseudochlorosis Infantum," and limit the term strictly to those anemias of a chlorotic type which are curable by the administration of iron alone.

He then gives a good deal of space to the so-called "goat's milk anemia," which has received much attention on the continent in recent years, and discusses the various theories of a special toxic action of goat's milk, most of which ascribe the "toxic" action to peculiarities in the fat portion. Baar raises the question whether there is really anything more than a quantitative difference between "goat's milk anemia" and "cow's milk anemia," and then delves into the whole question of the possible hemolytic action of fatty acids after absorption, the ideas of production of anemia by alkali or salt loss through soap stools and the absorption of the "giftfraktion" from the intestine. He describes in detail a number of his own observations and experiments on feeding, tending to show that "goat's milk anemia" can often be cured by the administration of richer mixtures of goat's milk, or goat's milk with cereal and vegetables, and that it is not cured by the simple change to cow's milk, unless a richer mixture is given. Similarly, "cow's milk anemia" was cured by the administration of richer mixtures of cow's milk, by suitable added food or by changing to richer mixtures of goat's milk.

Theoretical considerations and clinical study lead him to the final conclusion that "goat's milk anemia" and "cow's milk anemia" do not present essential differences, and that they are not due to toxins or to hemolytic agents but merely to "quantitative defects in the feeding regimen, general or partial undernourishment with carbohydrate-poor or vitamin-poor food." These defects lead to dystrophy, and in children constitutionally predisposed to anemia, they, together with repeated minor infections, lead to anemia. He considers the predisposition and the minor infections of prime importance.

In accordance with his ideas of pathogenesis he proposes that the nutritional anemias be classified as: (1) anemias from iron starvation (pseudochlorosis infantum); and (2) alimentary infectious anemias.

As to treatment, he points out the irrationality, from his point of view, of restricting the feeding of milk, but does not make any other special recommendations.

Baar's monograph covers his subject thoroughly. His conclusions, with which I am much in agreement, are well and clearly reasoned, and the booklet seems a worth while addition to the literature.

THE CAUSE AND CURE OF SPEECH DISORDERS; A TEXTBOOK FOR STUDENTS AND TEACHERS ON STUTTERING, STAMMERING AND VOICE CONDITIONS. By JAMES SONNETT GREENE, M.D., and EMILIE J. WELLS, B.A. Price, $4.50. Pp. 441, with 42 illustrations. New York: The Macmillan Company, 1927.

Books on disorders of speech written by and for physicians are infrequent in the English language. Therefore, books like this, written from the medical point of view, even though they are nontechnical and addressed to the general

public, possess a genuine medical significance. The subject of this volume is divided into (1) stammering ("stuttering"); (2) disorders of articulation (incorrectly called "stammering"), and (3) "voice conditions." Except for stammering, here called "stuttering," "cure" is given much more attention than "cause." The discussion of stammering is well worth study. This disorder, according to the authors, is due to a fundamental constitutional neuromental instability, and the peripheral speech disturbance is merely an incidental symptom. So much more important is the emotionality and excitability of the sufferer, compared to the peripheral speech disorder, that many pages are devoted to a detailed analysis of the mental phenomena, while a study of the nature of the peripheral phenomena is not made. The stuttering child, like the stuttering adult, is fundamentally neurotic, and the older stutterer is more neurotic only because of the disturbing effect produced on the mind by the disorder of speech.

The general psychology of the confirmed stammerer is presented with much elaboration and is well worth study by any student of the subject; and the practical advice to parents and teachers may well be widely read. But the attitude of finality assumed by these authors must be taken with much reserve. Until the extraordinary peculiarities of the peripheral speech disorder itself have been faced and understood, rather than evaded, as they are in this book, nothing can be assumed to be settled. Contrary to the belief of these authors, the key to the problem of stammering, as others hold, is to be found primarily in the unstable, developing, psychology of the child, coupled with his remarkably greater susceptibility, as compared with the adult, to a most extraordinary disturbance of the speech, namely stuttering. If a child starts stuttering, they say, he will eventually become seriously neurotic, even though at the start he is only mildly or not at all neurotic.

It may be that the narrow one-sided psychologic approach to the subject of stammering by these authors bears a relation to the somewhat inadequate, and sometimes inaccurate and hardly up to date, description of the physiology of speech, and the failure to discuss carefully the psychology of speech production, subjects that should form the strong basis of a book of this character. Much space is devoted to the correction of articulative disorders with many illustrative examples of speech. The book is well made and the illustrations are good.

LES VOMISSEMENT PÉRIODIQUES AVEC ACETONÉMIE. By A. B. MARFAN. Ed. 2. Price, 28 cents. Pp. 85. Paris: Masson & Cie, 1926.

At the outset, Marfan attempts to define the disease about which he writes, and he does so with the degree of success that has been attained by all others who have attempted the same thing; his definition is not a definition but a description in brief. The book that follows deals with the description in great detail from a clinical and pathologic standpoint; he then enters the field of physiology and attempts to explain it, and to bring all that is obscure into one satisfying hypothesis. Finally, there is a chapter on differential diagnosis and one on treatment.

Most writers have made two errors when dealing with this disease. One is an error that comes from too little attention to definition, and those who have made it have thought they have found the cause of recurrent or cyclic vomiting in chronic appendicitis, eye strain, postural defect and other conditions, when they have merely called attention to some cause of recurring attacks of vomiting. The other is an error that comes from too great attention to definition, and those who have fallen into this error have thought that because recurrent vomiting could be recognized clinically, it was a definite disease with definite pathogenesis. The truth is that one is dealing not with a definable disease, but with a group of symptoms and a train of occur-

rences which take place in a variety of conditions — one, clearly to be seen, another, obscure; one, part of the constitution of the child, another, environmental.

It is the attempt to treat the condition as a definite disease that makes the portion of the book dealing with the pathogenesis less satisfactory. Marfan naturally has his own hypothesis concerning the factors underlying the attack, and he allows his evaluation of the work of others to be influenced by the ideas he has formed from his own experience and from that of the colleagues whose work he accepts. He rejects Hilliger's and Knoepfelmacher's work on the blood sugar on the ground of inconstancy of results, but he puts forward a hypothesis of his own which, it seems to me, lacks proof as much as the attempted hypotheses of others he so easily rejects.

The book is most satisfactory in the chapters devoted to the clinical features of the condition, for the description is excellent and the bibliography is complete. No man is better fitted for the work of describing and reviewing this disease, and no man should be listened to with more respect than Marfan, who was the first to provide the means by which the attacks of cyclic vomiting could be recognized with certainty, and who, at the same time, gave the impetus for nearly all subsequent work.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION OF DISEASES OF CHILDREN

Chairman: Dr. Hugh McCulloch, 500 S. Kingshighway, St. Louis.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Minneapolis. Time: June 11-15, 1928.

AMERICAN PEDIATRIC SOCIETY

President: Dr. J. Claxton Gittings, 1828 Pine St., Philadelphia.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Washington, D. C. Time: April 30 to May 2, 1928.

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President: Dr. J. P. Crozier Griffith, 1810 Spruce St., Philadelphia.
Secretary: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Place: Minneapolis. Time: June 12, 1928.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.
Place: Undecided. Time: May or June, 1928.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. G. R. Pirie, 20 Madison Ave., Toronto.
Secretary: Dr. A. P. Hart, 1844 Bloor St. West, Toronto.
Place: Vancouver, B. C. Time: June, 1928.

SECTIONAL

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Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

President: Dr. Robert A. Strong, Pass Christian, Miss.
Secretary: Dr. Hugh L. Dwyer, Medical Arts Bldg., Kansas City, Mo.
Place: Memphis, Tenn. Time: Nov. 14 to 17, 1927.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Oscar Reiss, Westlake Professional Bldg., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 West 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, 537 Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 30 N. Michigan Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

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Secretary: Dr. F. J. Kinberger, 3601 Prytania St., New Orleans.

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Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. F. W. Schultz, University of Minnesota, Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. T. Wistor White, Lister Bldg., St. Louis.
Secretary: Dr. E. H. Rohlfing, 816 Beaumont Medical Bldg., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, 731 City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, 1036 Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr Harold L. Barnes, 1235 Dean St., Brooklyn.
Secretary: Dr. Charles A. Weymuller, 61 Greene Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St., and Grand Concourse, New York. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady, N. Y.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany, N. Y.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. William Ropes May, 8 East 66th St., New York.
Secretary: Dr. Stafford McLean, 17 East 71st St., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. Henry J. Gerstenberger, 2103 Adelbert Road, Cleveland.
Secretary: Dr. Charles W. Burhans, 2103 Adelbert Road, Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

President: Dr. M. A. Cox, 34 St. Clair Ave. West, Toronto.
Secretary: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Time: November 17, December 15, February 16 and March 15.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave., Memphis, Tenn.
Secretary: Dr. Arthur G. Quinlan, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Lucius D. Hill, Medical Arts Bldg., San Antonio.
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Place: Houston. Time: December, 1927.

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President: Dr. Howard Urbach, 1331 Grove Ave., Richmond, Va.
Secretary: Dr. W. Ambrose McGee, West End Medical Bldg., 2618 Grove Ave., Richmond, Va.
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Secretary: Dr. William B. McIlwaine, Petersburg, Pa.
Place: Danville, Va. Time: October 17, 1928.

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President: Dr. Roy M. Greenthal, 141 East Wisconsin Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

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